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Research article

Internal jugular vein distensibility in assessment of fluid responsiveness in donors of living donor liver transplantation

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ABSTRACT

Background: The concept of brain death is still not acceptable nor implemented in Egypt. Donor safety in liver transplantation is on the top of our priorities.

Purpose: The purpose of this study is to evaluate the effectiveness of using IJV distensibility as a reliable method for intraoperative assessment of fluid responsiveness.

Methods: A prospective observational study was conducted in Ain Shams university specialized hospitals. 40 donor candidates for right lobe hepatectomy for living donor liver transplantation were enrolled. During period of hypovolemia (T0) left IJV scanned and measured. After a given fluid bolus in the form of ringer acetate 5 ml/kg. ultrasonic and hemodynamic measurements were reassessed 10 min (T 10) after the fluid resuscitation.

Results: Highly significant changes in MABP, HR, and CVP ($p < 0.01$) were detected after fluid resuscitation, regarding the IJV distensibility it showed a highly significant reduction from baseline (T0) to post-resuscitation expansion ($P = 0.0001$). Baseline (T0) measurements showed no significant correlation between IJV distensibility and hemodynamic parameters ($P \geq 0.05$). Post-resuscitation values (T10) showed no significance correlation between HR and IJV distensibility ($P = 0.772$). On the other side it showed a highly significance negative correlation between MABP, CVP and IJV distensibility ($r = -0.390$, $P = 0.013$) and ($r = -0.332^*$, $p = 0.036$) respectively. The correlation between the percentages of change of IJV distensibility and hemodynamic parameters showed highly significant negative correlation between IJV distensibility and MABP ($r = -0.359$, $P = 0.023$) also with CVP ($r = -0.464$, $P = 0.017$). No difference was found regarding the HR ($P = 0.336$).

Conclusion: Organ transplantation centers with experience, CVP monitoring may not be necessary in highly selective patient population. IJV distensibility, a non-invasive and safe method can be used to guide fluid replacement in healthy donor.

1. Introduction

The concept of brain death is still not acceptable nor implemented in Egypt, although the Egyptian authorities had adopted a law for organ donation from deceased patient's in 2010, leading to severe shortage of adult organs. The total number of Living donor liver transplant (LDLT) till September 2016 are 2600 cases, preparation for LDLT program in Ain Shams University Specialized Hospital (ASUSH) started since 2001, our first case has been done in 2003. The total number of transplants performed is **283** by December 2016, and expected to increase.

Liver transplant is performed mainly for end-stage liver failure arising mainly from chronic liver disease due to hepatitis C virus inoculation.

Egypt has a very high prevalence of HCV and a high morbidity and mortality from chronic liver disease, cirrhosis, and hepatocellular carcinoma. Approximately 20% of Egyptian blood donors are anti-HCV positive. Egypt has higher rates of HCV than neighboring countries as well as other countries in the world with comparable socioeconomic conditions and hygienic standards for invasive medical, dental, or paramedical procedures [1].

Donor safety is on the top of our priorities as a team and it is widely recognized intraopertively during hepatectomy, there are several potential risks during the Perioperative period of this procedure, numerous studies reported their complications [2–7]. Major and minor complications, with associated rates of occurrences are illustrated in Table 1.

Generally, hepatectomy causes a major bleeding and high need of blood products requirement, which is one of the leading causes of post-

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Table 1
Postoperative donor complications by clavien grade [37,38].

Grade	Complication	N[a]	Rate[b] (%)
1	Atelectasis	16	3.70
	Ileus	15	3.46
	Fever	14	3.23
	Pleural effusion	11	2.54
	Hematemesis	1	0.23
	Intestinal obstruction	1	0.23
2	Need for blood transfusion[c]	14	3.23
	Pneumonia	7	1.62
	UTI	6	1.39
	Cellulitis	4	0.92
	Bacteremia	2	0.46
	C. difficile colitis	1	0.23
	Wound infection	1	0.23
3	Pneumothorax	2	0.46
	Intraoperative vessel injury	2	0.46
	Brachial plexus injury	1	0.23
4	Acute respiratory failure	3	0.69
	Cardiac arrest	2	0.46
5	Death	1	0.23

UTI = urinary tract infection.
[a] Patients can have multiple complications.
[b] Percent of total, N = 433.
[c] Nonautologous, nonintraoperative.

operative complications [8–10]. After several discussions with our surgical team we came to a conclusion that intraoperative fluid management aids to the reduction of the intraoperative bleeding during the procedure, adequate and guided fluid management is considered one of the important strategies to reduce the blood loss besides of the other anesthetic techniques like hemodilution, normovolemia [11], cell salvage usage [12], high Stroke volume variation (SVV) method [13], and low CVP technique [14], the last method is considered the most applicable, simpler, and cost effective technique which could be easier to be performed.

The first prospective report by Jones et al. [15] stated that maintaining a low CVP is a widely used method to minimize intraoperative blood loss [16,17], CVP is believed to reflect the hepatic sinusoid pressure, rendering it an effective indicator for reducing hepatic parenchymal congestion, thus reducing blood loss and controlling hepatic venous hemorrhage [18], it is well known that a target CVP during hepatic resection is 5 mmHg or lower has shown significant reduction of bleeding, morbidity and mortality [16–18].

However several studies have stated that CVP did not correlate with bleeding during the hepatectomy [19–21], Besides, there are potential fatal risks of low CVP strategies during hepatectomy include air embolism and tissue hypoperfusion [22], it was also reported by Jones et al. [15] that a small air embolism was noticed in two patients (5% of patients with low CVP), Another important issue should be taken into consideration; the complication of central venous catheterization is from 5% to 26% in all patients required treatment and monitoring [23].

Therefore, it took us to a new suggestion that a low CVP methods during hepatectomy may not be of a great benefit to the donors, we need more useful, safer and simpler methods for assessment of fluid management in order to reduce blood loss and subsequent morbidities during LDLT.

Point of care ultrasound imaging method of the IJV has been implemented for the evaluation of the CVP [24,25]. Lipton [25] identified the pulsation of IJV using the ultrasound pattern to estimate the CVP.

In this study, we evaluated donors candidates for hepatectomy in Living donor liver transplantation, we hypothesize that point of care ultrasound imaging of the IJV dispensability, would be correlated with the fluid status of the patients. The created database will help in establishing conclusion and recommendations that will help to improve the anesthetic plan, intraoperative management, and increase the donors' safety.

2. Methodology

This prospective blinded observational study was performed after obtaining approval from the ethical committee of the Ain Shams University from research ethical committee FWA 000017585, FMASU 313/2015, and registered in Clinical trials.gov; NCT03391037. Sample of 40 donors candidate for right lobe hepatectomy for living donor liver transplantation (LDLT) were included and written informed consent was taken, our main aim during preoperative preparation was to rule out any comorbidities or contraindications to donation by careful history taking, examination and investigations.

General anesthesia was induced in a standard technique with Fentanyl 2–4 μg/kg, Propofol 2 mg/kg and Rocuronium 0.6 mg/kg. Two large-bore peripheral and a right internal jugular central venous catheter were placed. Anesthesia was maintained with a balanced anesthetic technique, consisting of a volatile agent (Sevoflurane 0.7–1 MAC) and a mixture of air and oxygen (FiO2 0.4). For intraoperative analgesia, fentanyl infusion 1–2 μg/kg/h were used and fluids 3–5 ml/kg/h. Anesthetic management included the use of two forced air warming blankets for upper and lower extremities and an infusion blood warmer.

Intraoperative monitoring included ECG, invasive arterial blood pressure (left radial artery), noninvasive blood pressure, continuous central venous pressure (CVP), body temperature, oxygen saturation (SaO2), capnometry (EtCO2) and urine output (mL).

Recruitment of the patients (donors) depends on the presenting signs that led the anesthesiologist to decide if the patient's volume status was hypovolemic and in need for fluid replacement. This diagnostic criteria for volume assessment is usually a combination of heart rate (HR) more than 100b/min, mean arterial blood pressure (MABP) less than 50 mmHg, central venous pressure (CVP) less than 1 mmHg, and urine output hourly (UOP) less than 50 ml/h. During period of hypovolemia, all enrolled patients had left IJV scanned (T0) and measured by one anesthesiologist experienced in point-of-care ultrasound. This point-of-care anesthesiologist is not involved in the anesthetic management of the patient and blinded to the volume status of the patient values. Hypovolemic patients were given a fluid bolus in the form of ringer acetate 5 ml/kg. Ultrasonic and hemodynamic measurements are reassessed 10 min (T 10) after the fluid resuscitation.

Inclusion criteria included age of 20 years or older, candidate for donor right lobe hepatectomy for LDLT and volume assessment diagnosed as hypovolemia intraopertively by the anesthesiologist. Exclusion criteria were inability to scan IJV secondary to surgical dressing, hematoma formation after trial or placement of CVP catheter on left side, or inability for proper positioning. The IJV with a central venous catheter was not examined rather the opposite side was evaluated if no contraindications. No patients were excluded once enrolled and measurements were completed.

Ultrasound measurements were done using a linear transducer probe 6–13 MHz of the SONOSITE M-TURBO (USA). The IJV was measured using the B mode and the M mode.

The measurement technique

1. 30° head elevation.
2. Rotation of head slightly to right side to expose left IJV.
3. Place of linear probe horizontally across the neck and lateral to cricoid cartilage.
4. Applying minimal pressure to obtain adequate image.
5. Discrimination between 2 vessels by compressibility and color flow.
6. M mode to determine maximal and minimal diameter during a respiratory cycle (Figs. 1 and 2).
7. The IJV distensibility index was calculated as IJV maximal AP diameter during inspiration minus IJV minimal AP diameter during expiration divided by the minimal AP diameter during expiration.

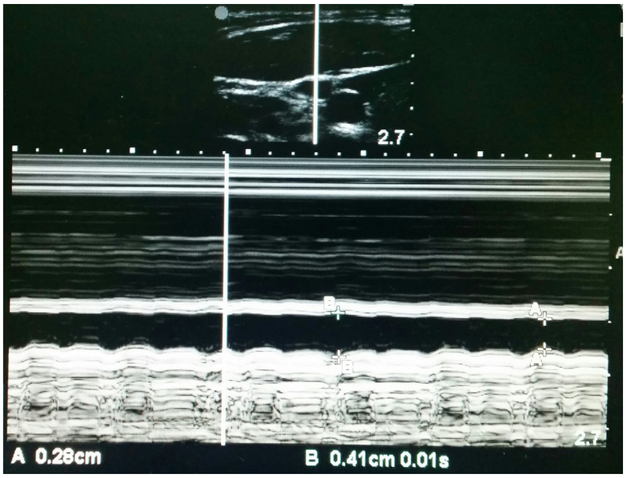

Fig. 1. Ultrasound images of the internal jugular vein during respiratory cycle in B mode and M mode. IJV distensibility during respiratory cycle with minimum AP diameter (A) maximum AP diameter, (B) measured in M mode. A high variability of IJV internal diameter is seen.

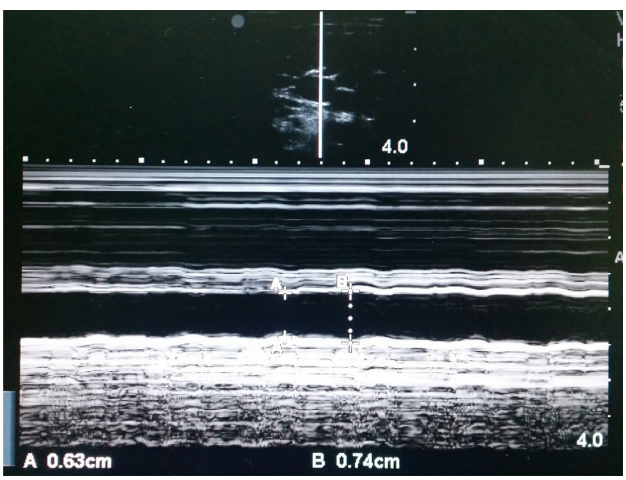

Fig. 2. Ultrasound images of the internal jugular vein during respiratory cycle in B mode and M mode. IJV distensibility during respiratory cycle with minimum AP diameter (A) maximum AP diameter, (B) measured in M mode. A less variability of IJV internal diameter is seen.

Primary outcome was the correlation between CVP and IJV distensibility. Secondary outcomes were IJV distensibility and hemodynamic measurements at T0 and T 10 and the correlation between IJV distensibility and both of MABP, HR and the correlation between the percentages of change of IJV distensibility and hemodynamic parameters.

2.1. Sample size

Using PASS program, setting alpha error at 5% and power 80%. Result from previous study [26] showed that the Pearson correlation coefficient between ultrasound measurement of the respiratory variation of IJV diameter with CVP measurement as (−0.306, with CI 0.061, −0.593). Based on this the needed sample is 31 cases rounded to 40 cases to compensate any dropouts.

2.2. Statistical analysis

Forty patients' data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric and median with inter-quartile range (IQR) when found non parametric. The comparison between two paired groups with quantitative data and parametric distribution were done by using Paired t-test while data with non parametric distribution were done by using Wilcoxon-Rank test. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the $p < 0.05$ and highly significant at the $p < 0.01$.

3. Results

From January 2016 to November 2017, we enrolled 40 healthy ASA 1 donors candidate for right lobe hepatectomy for living donor liver transplantation (23 males and 17 females, 25 to 35 median age and IQR age). Ultrasound evaluation and Hemodynamic measurements before (T0) and after (T10) fluid are illustrated in Table 2. Highly significant change in MABP, HR, and CVP ($p < 0.01$) were detected after fluid resuscitation, regarding the IJV distensibility it showed a highly significant reduction from baseline (T0) to post-resuscitation expansion (P = 0.0001). Baseline (T0) measurements are shown in Fig. 3 and Table 3 stated that there were not any significant difference correlation between IJV distensibility and other hemodynamic parameters (P ≥ 0.05). Post-resuscitation values (T10) shown in Table 4 stated that there was no significance difference correlation between HR and IJV distensibility (P = 0.772) on the other side it showed a highly significance negative correlation between MABP, CVP and IJV

Table 2
MABP, HR, CVP and IJV distensibility before and after fluid resuscitation.

		Before T0	After T10	% Change[a]	Test value	P-value	Sig.
		No. = 40	No. = 40	No. = 40			
MABP	Mean ± SD	58.40 ± 3.84	75.15 ± 5.07	27.70 (25–34.85)	–23.880[b]	0.000	HS
	Range	50–64	65–82	12.70–45.45			
HR	Mean ± SD	91.30 ± 8.13	82.30 ± 5.04	−10 (−13.06 to −6.17)	9.000[c]	0.000	HS
	Range	80–105	75–90	–23.81 to 2.50			
CVP	Median (IQR)	−1.00 (−1 to 0)	5.00 (4–5)	500 (400–600)	−5.593[b]	0.000	HS
	Range	−2.00 to 1.00	4.00–5.00	300–600			
IJV distensibility	Mean ± SD	51.10 ± 4.74	21.85 ± 4.02	−57.74(−62.25 to −54.12)	34.045[b]	0.000	HS
	Range	45–60	14–28	−70.91 to −41.67			

NS: Non significant; S: Significant; HS: Highly significant.
[a] Percentage change were presented as median with inter-quartile range (IQR).
[b] Paired t-test.
[c] Wilcoxon-Ranktest.

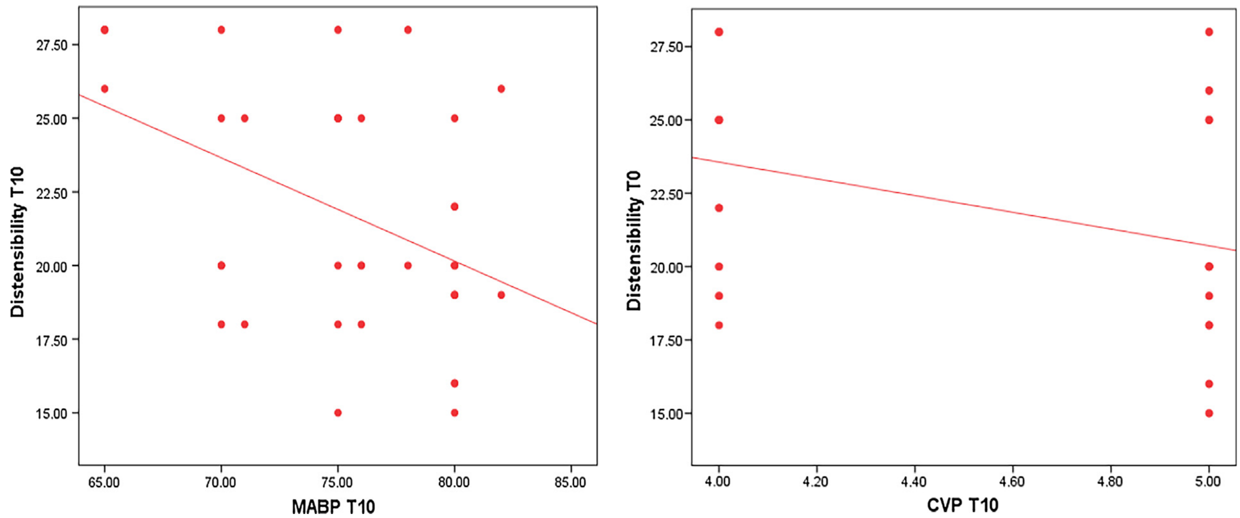

Fig. 3. Correlation between IJV distensibility and MABP and CVP at T 10.

Table 3
Correlation between IJV distensibility and other parameters at T0.

Before	Distensibility T0	
	r	p-value
MABP T0	0.306	0.055
HR T0	−0.250	0.120
CVP T0	−0.303	0.058

The previous table shows that there was no statistically significant correlation found between distensibility and the other studied parameters at T0.

Table 4
Correlation between IJV distensibility and other parameters at T10.

	Distensibility T10	
	r	p-value
MABPT10	−0.390*	0.013
HR T10	0.047	0.772
CVP T10	−0.332*	0.036

The previous table shows that there was no statistically significant correlation found between distensibility and the HR at T10 while the table also shows that there was highly statistically significant negative correlation between distensibility and MABP and also with CVP at T10.

* Percentage change were presented as median with inter-quartile range (IQR).

Table 5
Correlation between percent change in IJV distensibility and other parameters.

Percent change	IJV distensibility % change	
	r	p-value
MABP % change	−0.359*	0.023
HR % change	−0.156	0.336
CVP % change	−0.464*	0.017

The previous table shows that there was no statistically significant correlation found between distensibility and the HR at T10 while the table also shows that there was highly statistically significant negative correlation between distensibility and MABP and also with CVP at T10.

* Percentage change were presented as median with inter-quartile range (IQR).

distensibility (r = −0.390, P = 0.013) and (r = −0.332*, p = 0.036) respectively. We also studied the correlation between the percentages of change of IJV distensibility and hemodynamic parameters in Fig. 3 and Table 3 which showed highly significant negative correlation between IJV distensibility and MABP (r = −0.359, P = 0.023) also with CVP (r = −0.464, P = 0.017), no difference was found regarding the HR (P = 0.336) (Table 5).

4. Discussion

Taking a decision to donate a part or a portion of one's liver is a serious and life-threatening event. Our main purpose as a medical team is to ensure donor's safety all through the procedure especially when we have no established cadaveric programs for liver transplantation. It is obvious that right lobe hepatectomy can be done safely with minimal risks of serious Perioperative complications [27].

The main purpose of our study is to correlate between intraoperative ultrasound assessment of IJV distensibility and hemodynamic measurements in periods of hypovolemia as a method that can minimize fluid loads and subsequent hepatic sinusoidal congestion and further intraoperative bleeding, the correlation between IJV distensibility and other hemodynamic measurements as MABP, HR and CVP during periods of hypovolemia markedly increased the reliability of this predictive index. Management of intraoperative hypovolemia is of magnificent importance [28], but in partial hepatectomy patients (Donors) it should be guided to avoid hepatic congestion which will lead to undesirable bleeding and blood products requirements, which are included as one of the leading causes of post-operative morbidity and mortality [29,30].

Using our ultrasound approach we took some dynamic aspects of the patient response into consideration, like the minimum and maximum diameter of the IJV during ventilation, fixing the patient in the 30° position, decreasing intra-thoracic pressure by low PEEP values, cardiac preload actually did not increase due to the fixed position of the patient but there was a fact that the mechanical character of the IJV vessel wall relays on the patient's position [31].

Our static old fashion parameters, such as CVP, HR and MABP are poor indicators of fluid responsiveness as reported by Marik and his colleagues [32]. Respiratory variations of arterial pressures and aortic flow are considered desirable methods for rapid, simple, and easy measurement of fluid responsiveness [33]. Most of the studies combined the dynamic measurement as IJV distensibility and pulse pressure variation (PPV) aiming to improve the sensitivity and specificity of their calculations to predict fluid responsiveness, most of these studies evaluated the Cardiac index (CI) ability to respond to fluid challenges used ROC-curve to analyze the optimal threshold [34,35]. PPV is used to assess the LV response while IJV distensibility assessed the RV filling pressure and venous return; in our study we used IJV distensibility as a single method for assessment of the fluid responsiveness as we usually follow the low CVP techniques for fluid replacement aiming to decrease the hepatic congestion in addition to that nearly almost all of the donors cardiac functions are well assessed therefore we hypothesis that we can rely on assessment of the right sides filling pressure measurements in cases of hypovolemia without any need to assess the left sided pressures.

This technique of measuring the IJV diameter changes in donor patients is very easy and simple, with low training time and costs; also it is well established in insertion of the Central Venous catheter (CVC), in our results it showed strong correlation with other hemodynamic measurements on detecting fluid responsiveness in periods of hypovolemia during liver resection, perhaps this method could limit the use of CVC minimizing it's risks and hazards specially in Donors.

Niemann and colleagues studied monitoring of liver right donor hepatectomy patients with CVP and without; they concluded that the presence of CVP did not result in decreased intraoperative fluid administration, Length of post-anesthesia care unit and hospital stay. CVP monitoring did not appear to reduce blood loss when compared with patients without CVP monitoring. They recommended that centers with extensive experience, CVP monitoring may not be necessary in this highly selective patient population [19].

Analysis of the IVC collapse is also a predictive of fluid responsiveness which is not applicable to be measured during right lobe resection, which may suggest that our technique of IJV distensibility may still valid. The respiratory variation of the inferior vena cava and the right internal jugular veins are correlated and showed significant agreement [36].

There is a limitation in our work. Still we need to assess the IJV distensibility post-operatively in spontaneous breathing donors. We didn't reach the cutoff point in IJV distensibility for fluid responsiveness; we only correlate its reading with hemodynamic measurements.

5. Conclusion

Organ transplantation centers with experience, CVP monitoring may not be necessary in highly selective patient population. IJV distensibility, a non-invasive and safe method can be used to guide fluid replacement in healthy donor.

Conflict of interest

Nothing to disclose.

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