Contrast Enhanced Doppler Echocardiography in Chronic Obstructive Airway Disease to Assess Peak Pulmonary Artery Systolic Pressure

Saad Eldin Majeed
CABM

Abstract:
Background: Evaluation of pulmonary artery pressure is essential in the management of chronic obstructive airway disease.
Aim of the study: Evaluation of commonly used infusion fluids as contrast media to improve the attenuated transthoracic Doppler echocardiographic estimation of pulmonary artery systolic pressure in chronic obstructive airway disease patients with poor acoustic window.
Methods: Peak pulmonary artery systolic pressure (PPASP) in 60 healthy adults detected by trans-thoracic Doppler/echo was compared with that of similar number of difficult to image chronic obstructive pulmonary disease (COPD) patients before and after a contrast enhancement of the acoustic signal using commonly available infusion fluids (5% Glucose water, 0.9% normal saline, and 20% albumin and 5% albumin solutions) prepared by hand agitation.
Results: Contrast enhancement has significantly improved the color display and the spectral velocity envelope, and although albumin was the best contrast medium among the tested fluids, its diluted solution had reported the best profiles.
Conclusion: Hand agitated diluted albumin as contrast agent provide safe, inexpensive mean of improving the limited capabilities of the conventional Doppler/echocardiographic estimation of PPASP in COPD patients with poor acoustic window.

Key words: COPD, contrast echocardiography

Introduction:

Accurate and reproductive quantification of cardiac function is crucial in clinical medicine including chronic obstructive airway (COPD), a common clinical problem and the leading cause of chronic corpulmonale by causing sustained pulmonary artery hypertension with considerable right ventricular (RV) dilatation and dysfunction[1].

Cardiac catheterization is not ideal in assessing pulmonary hemodynamic in these patients, as it is an invasive technique and not free of complications [1]. Doppler-echocardiography has emerged as being more popular in this concept [2]; it is more widely available, repeatable, and relatively inexpensive, non-invasive technique [2-3]. The most accepted method for determining RV and pulmonary pressure has been the use of the modified Bernulli equation with tricuspid regurgitation peak systolic velocity [4-5]. This method determine accurately and reliably the systolic gradient between RV and right atrium[3], an essential step to calculate peak pulmonary artery systolic pressure (PPASP), but the problem with trans-thoracic imaging is the weak noisy signals commonly encountered in COPD patients due to poor acoustic window e.g. hyperinflated emphysematous chest, obesity[5]. Trans-esophageal echocardiography is an alternative to certain extent, but it is semi-invasive, time consuming and is usually not performed only to assess pulmonary hemodynamics [6]. Intravenous injection of contrast agent provide a cloud of micro bubbles acting as a strong acoustic refractor within normally echo free vascular lumens, salvaging the weak noisy signal and obtaining a clear velocity envelop[7].

The current work was conducted aiming for evaluation of commonly used infusion fluids as contrast media to assess PPASP in COPD patients who are difficult to image.

Patients & method:

A study was conducted in Doppler-echocardiography unit of the medical department/Al-Yarmouk Teaching Hospital., in the period from November, 2001 through February, 2002, to assess PPASP in 60 healthy adults (52-65 year-old) in comparison with age and sex matched group of COPD patients of difficult to image sustaining COPD (history, physical examination, chest X-ray, pulmonary function tests).

Pulse wave (P/W) Doppler echocardiography using commercial color/Doppler echocardiography system (Voluson 530 D of Kretz-Austria) equipped with mechanical phase array probe (2-4 MHz) was conducted, using long axis parasternal or subxephoid view to assess tricuspid regurgitation peak systolic velocity, color Doppler was used to align the sample volume within the TV area just in the RV inlet, and the insonation was kept to less than 30 degree [4].

A sharp spectral display was considered optimal when a clear window was obtained within the spectral envelope, attenuated signal with hazy peaks and boarders were weak signals, while the associated artifacts included in and/or out of the spectral display define the noisy signal. The color-Doppler signal used to align the sample volume was reliable if it lacked the aliasing effect [7].

The systolic pressure gradient across TV was estimated using modified Bernulli equation ($P=4V^2$, when V = maximum velocity of the systolic jet across the TV detected from the tricuspid regurgitation peak systolic velocity).

Right ventricular systolic pressure which stands for PPASP was estimated by the following formula: $RVSP=PPASP=4V^2+10$ mmHg as constant right atrial pressure [8].

The study was repeated in COPD patients using available infusion fluids (5% Glucose water (GW), 0.9% normal saline (NS), 20% albumin, 5% albumin) as contrast media prepared by hand agitation for more than 30 times using 2 syringes connected to stopcock [7-8]. The prepared solutions were injected from a peripheral vein (0.1 ml/kg) after decanting the visual bubbles [5, 7].

Data were analyzed using the available software package (SPSS-version 10) and then presented in simple measures of mean, standard deviation, range and median. The significance of difference was tested by paired t-test, with the use of P< 0.05 as the level of significance.

To determine the usefulness of the test as a diagnostic test, sensitivities and specificities were recorded with the likely positive and negative predictive values and the accuracy rate for the different contrast media, with cut-off point of 18.79 mmHg for PPASP among the healthy subjects.

Results:

Signal characteristics detected by color-Doppler echocardiography in healthy subjects and COPD patients and its behavior with the different contrast media were illustrated in tables 1 & 2.

Table-1: Signal characteristics, spectral display.

Spectral display	Healthy controls		COPD patients									
			Without contrast		With contrast							
					5% Glucose water		0.9% normal saline		20% albumin		5% albumin	
	No.	%	No.	%	No	%	No.	%	No.	%	No.	%
Weak	-	-	60	100%	56	93.3%	49	81.7%	-	-	-	-
Noisy	-	-	60	100%	60	100%	55	91.7%	23	38.3%	8	13.3%
Sharp	60	100%	-	-	-	-	-	-	60	100%	60	100%
Optimal	59	98.3%	-	-	-	-	-	-	13	21.7	54	90%
Suboptimal	1	1.7%	-	-	-	-	-	-	47	78.3%	6	10%
									P=0.0001*		P=0.052	

* Significantly different when compared with healthy controls.

Table-2: Signal characteristics, color coded signals (color Doppler).

Color coded signal	Healthy controls		COPD patients									
			Without contrast		With contrast							
					5% Glucose water		0.9% normal saline		20% albumin		5% albumin	
	No.	%	No.	%	No	%	No.	%	No.	%	No.	%
Reliable	59	98.3%	-	-	-	-	3	5%	40	66.7%	55	91.7%
Unreliable	1	1.7%	60	100%	60	100%	57	95%	20	33.3%	5	8.3%
Total	60	100%	60	100%	60	100%	60	100%	60	100%	60	100%
							P=0.0001*		P=0.0001*		P=0.094	

* Significantly different when compared with healthy controls.

Table 3 demonstrates the mean PPASP detected by Doppler echocardiography technique in healthy subjects and COPD patients who were difficult to image, before and after contrast enhancement of the acoustic signal.

The probable usefulness of contrast technique in improving the limitation of conventional Doppler-echocardiography in estimating PPASP is shown in tables 4 &5.

Table-3: PPASP (mmHg) for healthy controls and patients with COPD with and without contrast enhancement.

STUDY GROUPS		Peak pulmonary artery pressure		
		Mean ± SD	**Median**	**Range**
Healthy control		14.13±4.66	14.0	6-23
COPD patients	**Without contrast**	20.25±5.25	20.0	10-30
	5% Glucose water	21.65±5.66	20.5	12-32
	0.9% Normal Saline	23.98±5.83	22.5	15-36
	20% albumin	29.15±5.4	28.0	20-42
	5% albumin	32.77±5.25	31.0	25-47

Table-4: PPASP (mmHg) for healthy controls and patients with COPD with and without contrast enhancement with a cut-off point of 18.79(mean PPA of healthy controls ± SD).

STUDY GROUPS		**Above**	**Below**	**Sensitivity (%)**	**Specificity (%)**	**Positive predictive value**	**Negative predictive value**	**Accuracy**
Healthy control		12	48	-	-	-	-	-
COPD patients	**Without contrast**	36	24	60	80	75	66.7	70
	5% Glucose water	38	22	63.3	80	76	68.6	71.7
	0.9% Normal Saline	50	10	83.3	80	80.7	82.8	81.7
	20% albumin	60	-	100	80	83.3	100	90
	5% albumin	60	-	100	80	83.3	100	90

Table-5: The significance of differences in peak pulmonary artery pressure (mmHg) for patients with COPD.

	Without contrast	5% Glucose Water	0.9% Normal Saline	20% albumin	5% albumin
Control	P=0.0001	P=0.0001	P=0.0001	P=0.0001	P=0.0001
Without contrast		P=0.0001	P=0.0001	P=0.0001	P=0.0001
5% Glucose water			P=0.0001	P=0.0001	P=0.0001
0.9% Normal Saline				P=0.0001	P=0.0001
20% albumin					P=0.0001

Discussion:

The improvement in color Doppler imaging helped to find the real topographic origin of the signals registered, and to avoid an ambiguous gate while aligning the sample volume within the tricuspid valve area (Tables 1&2). Consequently improving the attenuated spectral envelope and the quantitative information were obtained with a better diagnostic confidence (Tables 1 & 4).

The study demonstrated the potential of Doppler/echocardiography to quantify PPASP (Tables 3 & 4), and that significant improvement in the calculation could be made using simple contrast media to overcome the difficulty encountered in COPD patients due to poor acoustic window (Table 5).

The unique feature of the fluids included in the study as contrast media is that, they all are intravenously injectable, iso-osmolar, non-toxic, chemically inert and readily accessible in clinical practice. The differences in their Doppler features (Tables 1 & 2) appear to be related to their properties as liquids.

Two factors influencing the ability of any liquid to act as a contrast agent [8-9]: the number of micro-bubbles created by mechanical agitation of the liquid, and is directly proportional to the viscosity of that liquid, which in turn the function of its density. Liquid with higher viscosity generates denser acoustic cloud due to greater number of crowded micro-bubbles [8-9].

The second factor influencing the liquid as an acoustic contrast is the size of the created micro-bubbles which is inversely related to their surface tension. Larger bubbles suffer low surface tension, are more fragile, and less stable in liquid.

Thickness and flexibility of the bubble shell are additional properties influencing the liquid stability as a contrast medium, and both are affected by the above mentioned factors[9], suitably thick and flexible micro-bubbles are more stable and survive longer when traversing the circulation[7,9]. Ultrasonically only bubbles larger than 6 micrometer in diameter can be visualized [7].

Agitated albumin produces micro-bubbles with mean diameter of 5-8 micrometer with theological properties similar to RBC, making it a suitable acoustic contrast (Tables 3 & 5). Due to its higher viscosity, agitation of undiluted albumin creates larger number of micro-bubbles generating hyperdense acoustic cloud which might have deleterious effect on the acoustic signal rather than improving its resolution (Table 1). The acoustic cloud generated this way may act as a scattering barrier dissociating the ultrasound beam leading to spectral blooming and hazing effect, sub-optimizing the Doppler display. Diluted albumin is less viscous and the cloud of echoes it produces is more reliable in enhancing both the color and spectral signals (Tables 1 & 4).

On the other hand, the larger sized bubbles created by agitating normal saline (low surface tension) might smashed down to smaller bubbles by the ultrasound beam or when traversing the circulation improving the acoustic refractoriness of the generated cloud as the number of the created micro-bubbles increases, a suggestion which might explain the relatively higher potential of normal saline as a contrast medium in comparison with 5% glucose water.

The study provides safe, inexpensive mean of enhancing the capabilities of trans-thoracic Doppler echocardiographic technique in estimating PPASP in COPD and eliminating the need to non-echocardiographic technique or the use of manufactured ultrasound contrast agents that would only add to the cost of health services and expose the patient to potential side effect.

In conclusion, contrast enhancement of the weak noisy signal in COPD patients is possible using hand agitated infusion fluid, particularly 5% albumin. It provide simple, safe, inexpensive mean of improving the trans-thoracic Doppler echocardiography capabilities in COPD patients with poor acoustic window.

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From Med. Dept. Coll. of Med., Al-Mustansiriya Univ.