Accuracy of current non-invasive methods in estimating invasively obtained aortic coarctation gradients

Wejdan Khaled Ba-Atiyah, Riad Abou Zahr, Zaheer Ahmad, Yahia Mohamed El Mahdi, Mohammed Omar Galal.
Department of Pediatrics, Section of Pediatric Cardiology, King Faisal Specialist Hospital & Research Center, Jeddah, Saudi Arabia.

ABSTRACT:

Aims: To understand the accuracy of non-invasively obtained blood pressure gradie vs Doppler gradient) with an invasively measured pressure g

Study design: Retrospective study.

Place and Duration of Study: Department of Pediatrics, Section of Pediatric Cardiology, King Faisal Specialist Hospital & Research Center, Jeddah, Saudi Arabia, between Jan, 2010 till Jan, 2020.

Methodology: A retrospective study of patients with CoA who underwent catheterization between Jan, 2010 till Jan, 2020 was performed. Cuff BP gradie Doppler echocardiography were measured prior to cardiac catheterization and afte when an intervention was performed. Student t test and Bland-Altman analys per

Results: 55 patients with aortic coarctation underwent 92 cardiac catheterizations. them 75 needed interventions. This resulted in a total of 162 cardiac catheterizati them 67 pressure gradients included in the analysis. There was no statistically sig difference between mean Doppler measurements and invasively derived catheter g (p=0.12). In contrast peak Doppler measurement ($p < 0.00001$) and cuff blood p gradients (p=0.03) showed significant differences to the cath gradient. We found t blood pressure gradients accurately reflected cath measurement in native COA (p=0. in those who weigh less than 10 kg (p=0.67). Mean Doppler measurements had tendency for underestimation. Peak Doppler gradient and cuff pressure gradient overestimated cath measur

Conclusion: The mean Doppler echocardiography seems to be the most accurate the other noninvasive methods in use to estimate severity of aortic coarctation. It p reasonable agreement with the invasively obtained aortic coarctation gr

Keywords: Aortic coarctation, Doppler echocardiogram, cardiac catheterization, cuff blood pressure.

1. INTRODUCTION

Several non-invasive methods have been used to measure the gradient across the coarctation site before any intervention or to identify residual obstruction after surgical repair or transcatheter intervention. This is most commonly done by measuring systolic four limbs blood pressure gradient between upper and lower limbs measured by sphygmomanometry. Additionally, it is confirmed by two dimensional Doppler echocardiography which estimates the peak instantaneous pressure gradient across the narrowed area using modified Bernoulli's principle [1]. Intervention is generally advocated for a peak-to-peak gradient ≥ 20 mmHg at cardiac catheterization in patients with biventricular circulation and more than 10 mmHg in single ventricle palliated patients [2, 3]. According to severity, patients either will be sent to cardiac catheterization to assess the gradient across the coarctation and decide on the need for any intervention such as balloon dilation or stent angioplasty. On different occasions especially in neonates and some infants, patients will go directly to surgery [4-6].

In clinical settings, cardiac catheterization has been the gold standard for definitive evaluation of a gradient across the coarctation [7, 8]. CT angiography has been recommended to judge the severity and also the type of the aortic coarctation before embarking on any sort of intervention [9, 10].

It has been reported that Doppler gradient across the aortic narrowing seems to overestimate the gradient obtained during cardiac catheterization [1, 11]. Some suggested that taking the blood pressure gradient measured by cuff, especially in the younger age group, does not truly reflect the invasive gradient [12]. The utility of this approach in cases of re-coarctation has also been questioned. There is limited data to whether non-invasive gradient estimates are valid after intervention done to aortic coarctation [1, 8, 13].

In this study, we attempted to assess the relation of different noninvasive methods with invasive blood pressure gradient in patients with coarctation of the aorta. At the same time, we examined other factors (like weight of patient, functional single ventricle etc) that potentially have an effect on the accuracy of the gradient. Furthermore, we investigated whether a previous coarctation intervention affected the accuracy of non-invasive blood pressure gradient estimation.

This study has a potential impact on clinical evaluation and management of patients with aortic coarctation. It could help in decision making regarding the need for any intervention.

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

A single center, retrospective chart review study was initiated using demographics, noninvasive cuff blood pressure gradient, echocardiography and cardiac catheterization data-bases. We studied patients who underwent cardiac catheterization between Jan, 2010 till Jan, 2020.

2.1 INCLUSION CRITERIA:

All patients with the diagnosis of coarctation, aortic arch obstruction, or aortic arch hypoplasia who underwent cardiac catheterization and who had a pre- and/or post-procedure Doppler echocardiogram with four limbs blood pressure were included in the study.

2.2 EXCLUSION CRITERIA:

We excluded from the study premature infants less than two kg, patients with diffuse arch hypoplasia (transverse and ascending arch hypoplasia), patients with multiple levels of arch obstruction, patients with greater than mild aortic valvar stenosis > 30 mmHg, or greater than mild aortic insufficiency (P1/2t < 400 ms), patients with moderate to severe (LV) dysfunction with ejection fraction < 40% and patients with patent ductus arteriosus (PDA) or systemic to pulmonary shunts.

All data were collected from the patient's chart and reports that are stored in the electronic medical record. As for the Echo Doppler gradients they were measured by the investigators using the images stored in the echo database.

The study was approved by the Institutional Review Board.

The following data were collected: demographic data, presence of extra cardiac anomalies or syndrome, associated cardiac lesions, univentricular vs biventricular, date and type of prior intervention, patient age and weight at the time of cardiac catheterization.

2.3 CUFF BLOOD PRESSURE:

For cuff blood pressure measurement, the Dinamap blood pressure device (Dinamap ProCare 400, GE Medical Systems, Milwaukee, WI, USA) was used. The cuff sizes were chosen according to the patient’s age/weight and limb size. The blood pressure was measured from both arms and calves. The difference between blood pressure of upper and lower limbs was calculated and used in comparison to the invasively obtained gradient. Cuff blood pressure gradients were measured prior to cardiac catheterization and then re-measured in case a patient had undergone interventional cardiac catheterization (balloon dilation/stent).

2.4 ECHOCARDIOGRAM:

Echocardiograms were performed either while the patient was awake or under conscious sedation according to the patient's age and cooperation. Standard pediatric echocardiographic images specifically subcostal, and suprasternal notch views were obtained using the transducer appropriate for the patient’s size. All studies were performed using models (IE33; Philips Medical Systems, Eindhoven, The Netherlands).

Echocardiographic measurements included aortic arch peak and mean instantaneous pressure gradients. The left ventricular function was calculated using shortening fraction (SF) and ejection fraction (EF). The presence or absence of diastolic forward flow was assessed qualitatively based on the slope of the Doppler flow pattern and whether it returned to baseline during diastole. The Doppler peak instantaneous pressure gradient was calculated using the simplified Bernoulli equation – peak instantaneous pressure gradient = $4v^2$ [1]. The Doppler mean instantaneous pressure gradient was performed by tracing the Doppler waveform to average the instantaneous gradients throughout systole.

In case the patient underwent cardiac catheterization with intervention (balloon dilation, stenting), Doppler echocardiography was performed pre and post cardiac catheterization. Peak & mean instantaneous pressure gradients were measured.

2.5 CARDIAC CATHETERIZATION:

Cardiac catheterization was performed either under conscious sedation or general anesthesia. The peak-to-peak gradient was measured in all cases using the retrograde pull-back technique. The site and shape of coarctation were recorded after performing angiography. When needed intervention was done. In this case pre and post intervention (balloon dilation, stenting) pull back gradients were recorded.

Initial peak-to-peak gradients before and post intervention were compared with pre-catheterization cuff blood pressure gradients, echocardiogram peak and when available mean instantaneous pressure gradients.

2.6 STATISTICAL ANALYSIS:

We used standard descriptive statistics to describe the study variables, including means, standard deviations and median. The blood pressure cuff gradient and Doppler echocardiogram peak and mean instantaneous pressure gradients were compared with cardiac catheterization peak-to-peak pressure gradients using the two tailed Student’s t test. P value of < 0.05 was considered statistically significant. Agreement between each non-invasive method and catheterization was described using Bland-Altman plot analysis [14].

Data were analyzed according to the following parameters: patients weight (<10kg or >10 kg), native coarctation, post intervention coarctation (Balloon dilatation, stent) and functional physiology (Univentricular, biventricular track).

3. RESULTS AND DISCUSSION

3.1 RESULTS:

A total of 55 patients (23 males and 32 females), with a diagnosis of aortic coarctation were identified and included in our study. These 55 patients underwent a total of 92 cardiac catheterizations. At the time of the first cardiac catheterization, the mean age was 5 years (range 28 days to 33 years), mean weight was 20 kg (range 2 kg to 82 kg).

Among 92 catheterizations, 75 underwent intervention in the form of balloon dilation, stent angioplasty or in one patient surgery. This resulted in a total of 162 cardiac catheterization gradients (Figure1).

Of 162 cardiac catheterization readings, only 67 had BP and echocardiogram Doppler pressures were available for comparison.

Among the 67 cardiac catheterization included, 23% had native coarctation, 77% had a history of previous intervention (balloon dilatation, stent or aortic arch reconstruction surgery). 46% of patients at the time of the cardiac catheterization were below 10 kg. The majority of patients (82%) had biventricular physiology while (18%) had single ventricle physiology (Table 1, Figure 1).

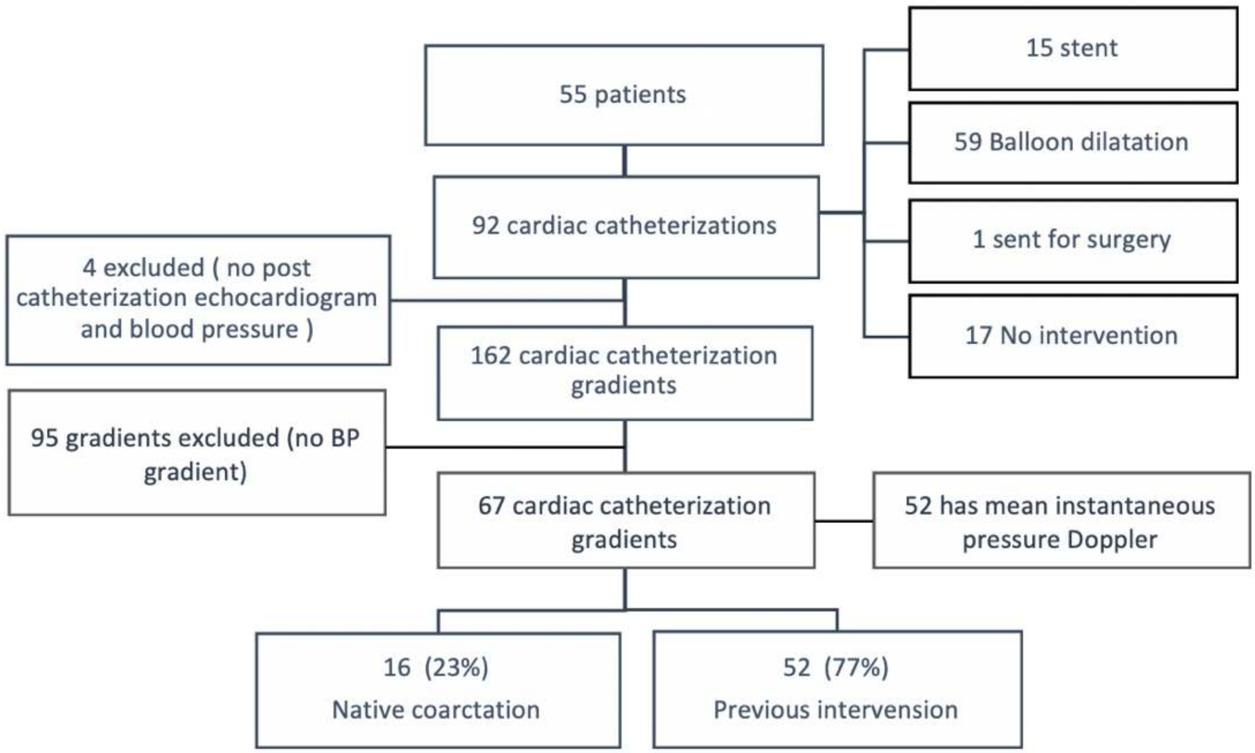

Figure 1: Diagram depicting the total number of patients and the number of comparative procedures studied.

BP, Blood pressure.

Table 1: Demographic data and characteristics of the patients included in the study.

Among 55 Patients:	Frequency	Percentage (%)
Male	23	42
Female	32	58
Among 92 cardiac catheterization Procedures:	**Mean**	**Range**
Age (year)	5	0.076 - 33
Weight (kg)	20	2 - 82
Among 67 catheterization gradients readings:	**Frequency**	**Percentage (%)**
Below or equal 10 kg	31	46
More than 10 kg	36	54
Native coarctation	16	23
Previous Intervention	52	77
Single ventricle track	12	18
Biventricular track	55	82

3.1.1 Cuff blood pressure gradients:

The average cuff Blood pressure gradients were available in all included patients who underwent cardiac catheterization (67 gradients). In these measurements, the average Cuff Blood pressure gradient was 30 ± 15 mmHg (Table 2).

Table 2: Comparison between Blood pressure cuff gradient, Doppler echocardiogram and cardiac catheterization gradients.

	Average Gradient (mmHg)	Standard Deviation (mmHg)	Median Gradient (mmHg)
All 67 pressure gradients:			
Cuff BP Gradient	30	15	29
Peak Doppler Echocardiogram	45	15	45
Mean Doppler Echocardiogram	21	8	20
Catheter gradient	25	17	24
Patients with Native CoA:			
Cuff BP Gradient	35	19	33
Peak Doppler Echocardiogram	51	14	52
Mean Doppler Echocardiogram	23	7	25
Catheter gradient	30	17	31
Patients with previous CoA intervention:			
Cuff BP Gradient	22	16	19
Peak Doppler Echocardiogram	35	16	35
Mean Doppler Echocardiogram	19	10	21

Catheter gradient	16	10	18
Body weight < 10 kg:			
Cuff BP Gradient	28	18	28
Peak Doppler Echocardiogram	46	18	49
Mean Doppler Echocardiogram	19	9	20
Catheter gradient	27	20	25
Body weight > 10kg:			
Cuff BP Gradient	32	14	32
Peak Doppler Echocardiogram	45	12	45
Mean Doppler Echocardiogram	23	6	23
Catheter gradient	26	14	22
Patient with single ventricle physiology:			
Cuff BP Gradient	26	14	24
Peak Doppler Echocardiogram	39	19	39
Mean Doppler Echocardiogram	20	10	19
Catheter gradient	16	14	14
Patient with Biventricular physiology:			

Cuff BP Gradient	31	16	31
Peak Doppler Echocardiogram	46	14	47
Mean Doppler Echocardiogram	21	7	21
Catheter gradient	27	17	24

**BP, Blood pressure; CoA, Coarctation of aorta.*

By using two tailed students t test the correlation between cuff gradient and catheter measurements showed a p=0.034 (Table 3). Bland-Altman plot analysis revealed an overall bias between cuff and cath blood pressure gradient of 5 mmHg with a standard deviation of 19mmHg, suggestive of a small tendency of cuff gradient to overestimate. The 95 % limits of agreement between cuff and cath gradients were 42 and -32 (Figure 2).

Table 3: Correlation of Cuff blood pressure, Doppler gradient and cardiac catheterization gradients considering factors assumed to have effect on accuracy of predicting the gradient (P value of < 0.05 was considered statistically significant).

	Cuff BP VS catheter gradient	Peak Doppler Echocardiogram VS catheter gradient	Mean Doppler Echocardiogram VS Catheter gradient
All 67 pressure gradients	0.03	< .00001	0.12
Weight < 10 kg	0.67	< .00001	0.10
Weight > 10 kg	0.008	< .00001	0.75
Native COA	0.40	< .00001	0.22
Previous Intervention	0.04	< .00001	0.32
Single ventricle track	0.06	0.0001	0.40

Biventricular track	0.13	< .00001	0.05

* *BP, Blood pressure; CoA, Coarctation of aorta*.

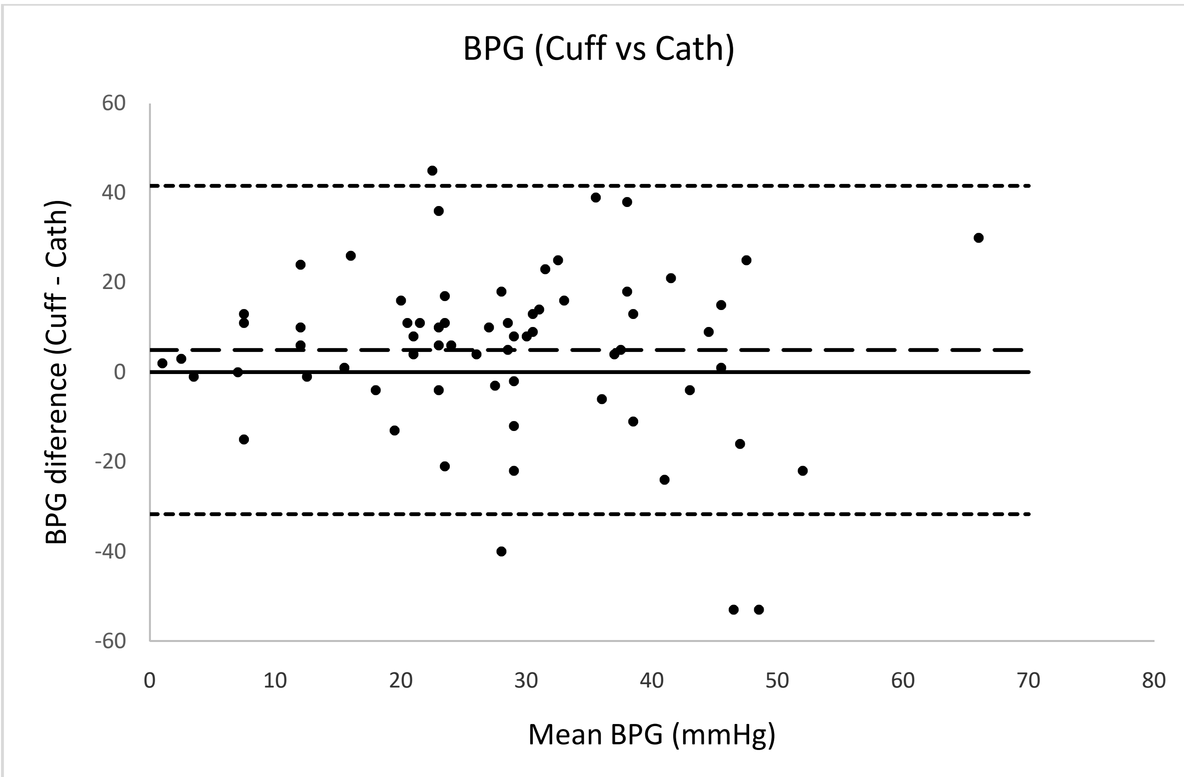

Figure 2: Bland-Altman plot analysis demonstrates moderate agreement with wide scatter between cuff and cath BP gradients. The small-dashed lines indicate the upper and lower 95% limits of agreement between the two measurements. The large-dashed line represents the mean difference. The solid line represents zero (no bias).

** BPG, Blood pressure gradient.*

3.1.1.1 Native coarctation vs post intervention coarctation

The results of patients with native coarctation (n=16) did not differ from the cath gradient (average cuff gradient 35 ± 19 mmHg vs average cath gradient (30 ± 17 mmHg); (p =0.41). This indicated that in native coarctation, cuff gradient can reliably estimate catheterization gradient.

The average cuff gradient among the post intervention patients (n=51), was (22 ± 16 mmHg), and was significantly different from the gradient obtained at cardiac catheterization (16 ± 10 mmHg), (p=0.04).

3.1.1.2 Body weight < 10 kg vs > 10 kg

Comparing the result of patients whose weight were less than 10 kg (n=31) with those whose weight were more than 10 kg (n=36), the cuff gradient of the patients with less than 10 kg did not differ significantly from the gradient obtained at cardiac catheterization. This suggested that in patients with weight less than 10 kg, the cuff gradient can reliably estimate the catheterization gradient (p=0.67).

3.1.2 Doppler echocardiogram:

Echocardiograms were obtained in all patients, pre and post interventions, when needed.

The average peak instantaneous pressure gradient across the isthmus of the 67 patients was 45 ± 15 mmHg (Table 2).

By using two tailed student t test the correlation between peak Doppler measurements

and catheter measurements showed a p<0.00001, indicating highly significant differences between both measurements. Hence, the Doppler peak measurement did not reflect the gradients obtained during cardiac catheterization (Table 3).

Bland-Altman plot analysis revealed an overall bias between peak echo Doppler and cath BPG of 18 ± 14 mmHg suggesting more tendency of peak echo Doppler for overestimation. The 95 % limits of agreement between peak echo and cath gradients were 46 and -9.6 (Figure 3).

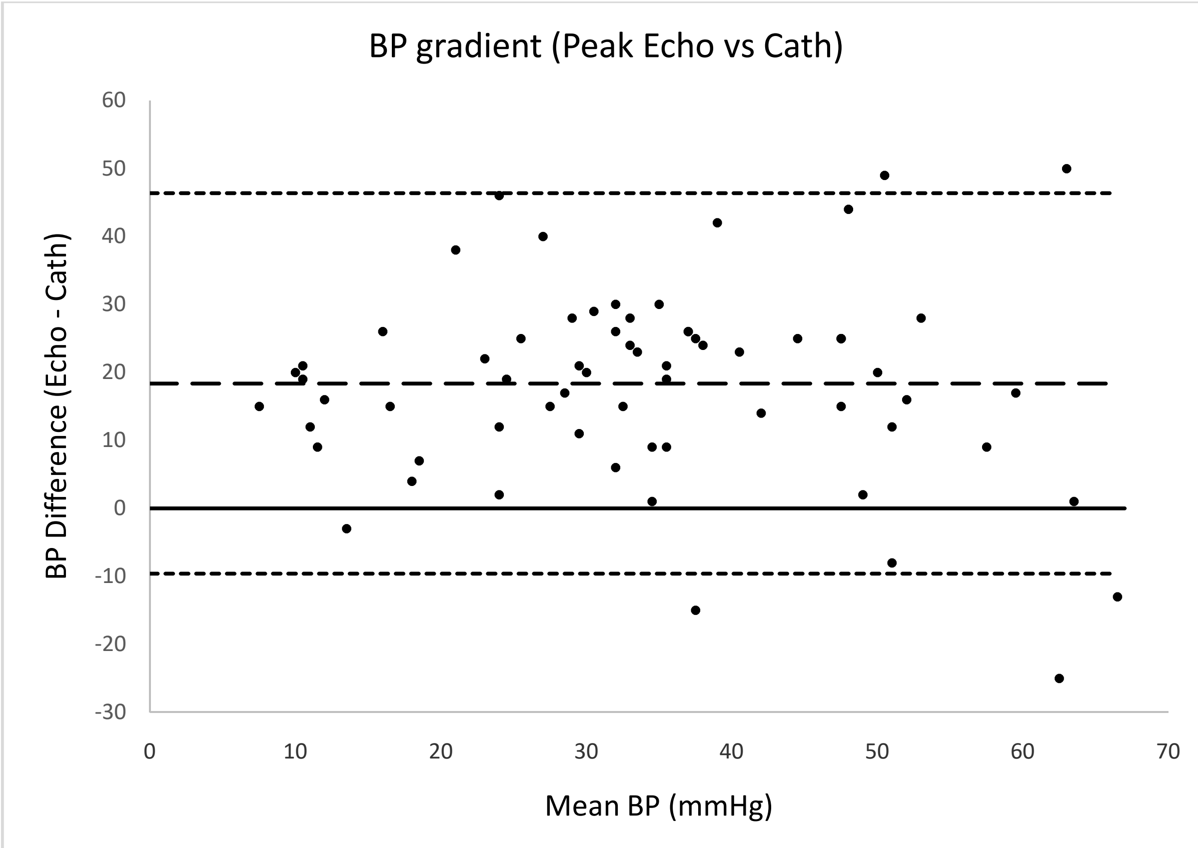

Figure 3: Bland-Altman plot analysis demonstrates weak agreement with wide scatter between peak echo and cath BP gradients. Note scatter increases with increasing BP gradients. The small-dashed lines indicate the upper and lower 95% limits of agreement between the two measurements. The large-dashed line represents the mean difference. The solid line represents zero (no bias).

** BP, Blood pressure.*

Of the 67 patients analyzed, it was possible to measure mean instantaneous pressure Doppler on 52. The average mean instantaneous pressure gradient was 21 ± 8 mmHg.

By using two tailed students t test the correlation between mean Doppler measurements and catheter measurements showed p=0.12, indicating that there are no significant differences between them and that the mean Doppler measurements can effectively estimate catheter measurement (Table 3). Bland-Altman plot analysis revealed an overall bias between mean echo Doppler and cath blood pressure gradient of - 3.3 mmHg with a standard deviation of 15 mmHg, suggesting a small tendency of mean echo Doppler to underestimate the invasively obtained gradient. The 95 % limits of agreement between mean echo Doppler and cath were 26 and -33 (Figure 4).

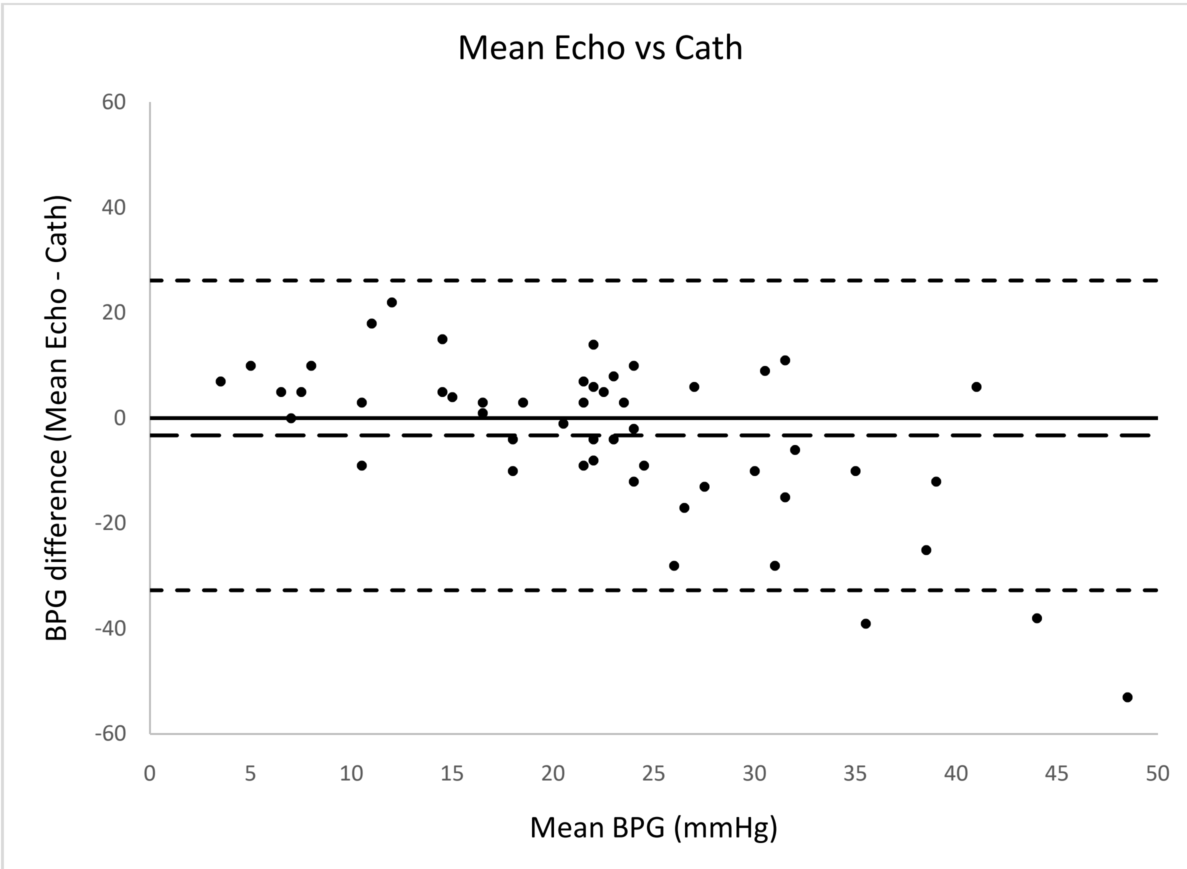

Figure 4: Bland-Altman plot analysis demonstrates good agreement between mean echo and cath BPG. Note the tendency to underestimate increased at higher gradients. The small-dashed lines indicate the upper and lower 95% limits of agreement between the two measurements. The large-dashed line represents the mean difference. The solid line represents zero (no bias).

** BPG, Blood pressure gradient.*

There was no difference between the patients with native COA and those with post COA intervention.

3.1.3 Cardiac catheterization:

The average peak-to-peak pressure gradient measured in 67 readings at cardiac catheterization was 25 mmHg ± 17 mmHg (Table 2).

It is worth mentioning that the median gradients for Cuff, Doppler and catheterization did not differ much from the mean values; indicating normal distribution of the data.

3.2 DISCUSSION:

Coarctation of the aorta varies in its presentation and can pose diagnostic and therapeutic challenges. There are many variables which are used to predict catheterization gradients and hence deciding about the timing of any necessary intervention. To assess the severity of aortic coarctation, initially it can be predicted by using clinical examination, non-invasive methods as cuff blood pressure gradient of the four limbs and Doppler echocardiogram peak and mean instantaneous pressure gradients [2]. After the non-invasive assessment, the decision for any intervention remains challenging. Occasionally, in our experience, one of these methods gave a very high gradient, while the catheterization did not. Hence, the aim of our study was to try to understand under which conditions those non-invasive methods would best reflect the invasively obtained gradient across the coarctation.

3.2.1 Our Findings:

We found that the Doppler estimated **mean** instantaneous pressure gradient correlated more closely with directly obtained catheter measurement as compared to Doppler **peak** instantaneous pressure gradient and cuff blood pressure gradient. Peak Doppler echocardiography gradient had more tendency for overestimation, than cuff blood pressure gradient. On the contrary, mean Doppler echocardiogram gradient had a small tendency for underestimation. This was more pronounced with increasing gradients.

We sought to understand which factor-if any-could have an effect on the accuracy of estimating the invasive coarctation gradient. Variables including weight, native vs post intervention of coarctation, and the patient with biventricular vs single ventricle track were assessed to understand their impact. Interestingly, we found that cuff blood pressure gradients still accurately reflected invasive measurements in patients with native COA and on those who weigh less than 10 kg. In contrast, the peak Doppler echocardiography overestimated the cath measurements in all groups. The type of physiology (biventricular vs single ventricle track) had no significant effect on the measurements (Figure 5).

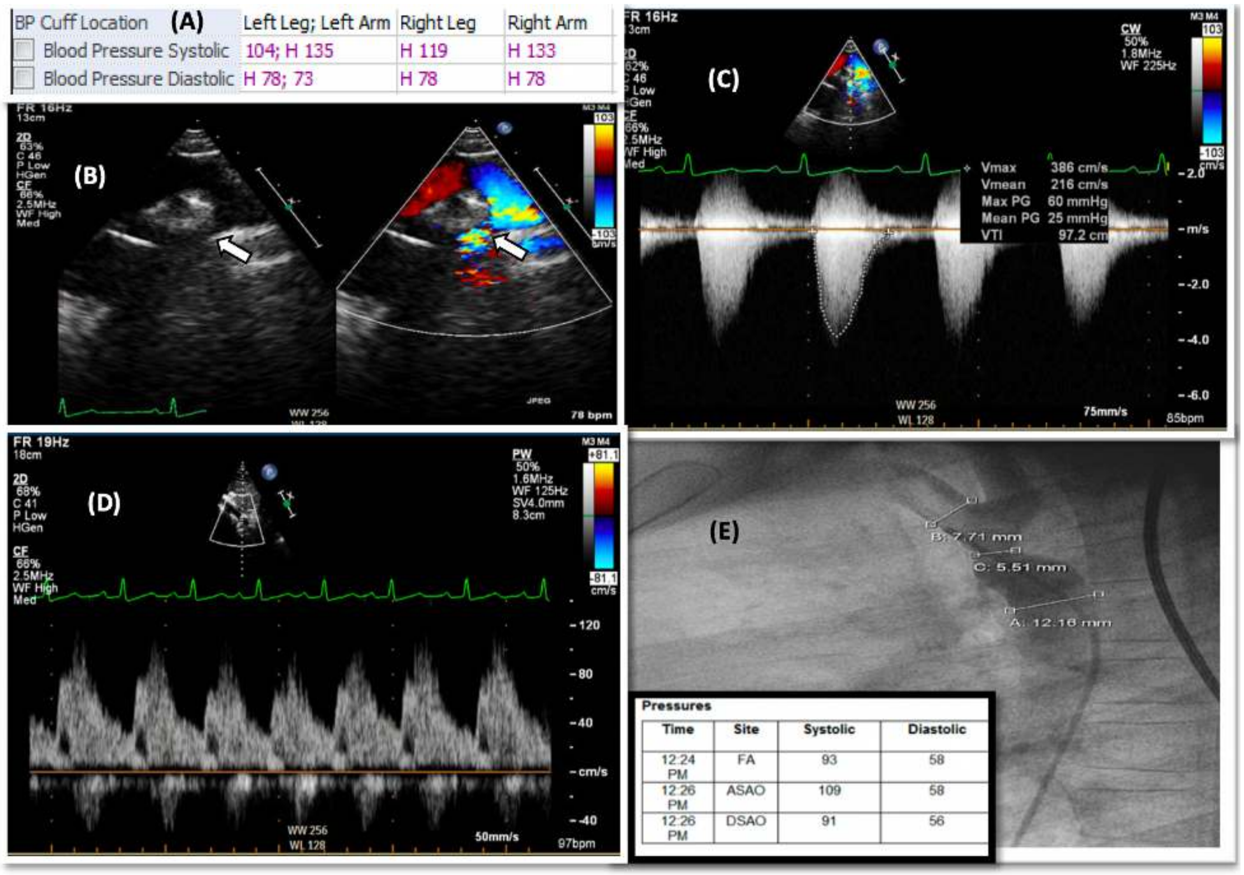

Figure 5: A case of a seven years old boy known to have coarctation and bicuspid aortic valve with no aortic stenosis, with a history of previous balloon dilatation. (A) Four limbs cuff blood pressure shows gradient of 29 mmHg, (B) Transthoracic echocardiogram suprasternal view of aortic arch shows the aortic coarctation site (arrow) with color flow turbulence at the site of CoA (arrow). (C) Continuous wave Doppler interrogation across the stenotic segment shows peak instantaneous gradient of 60 mmHg. (D) Pulse Doppler of abdominal aorta from subcostal views shows damped trace with diastolic tailing. (E) Aortogram shows discrete aortic coarctation distal to the left subclavian artery with peak to peak gradient of 18 mmHg.

3.2.2 Literature review:

Christopher et al. (2018) conducted a retrospective study with 68 patients of whom 84% underwent intervention during catheterization. Most peak Doppler obtained gradients showed moderate correlation (r = 0.503–0.617, p<0.001) with gradients obtained at catheterization. It was found that noninvasive four extremity blood pressure gradients correlated significantly only if peak-to-peak gradient was ≥ 20 mmHg [15]. Wisotzkey et al. (2015) carried out a retrospective comparison of cardiac catheterizations and pre- and post-catheterization echocardiograms in 60 patients with 34 (57%) native coarctation and 26 (43%) aortic re-coarctation. They found that in all cases, the Doppler peak instantaneous pressure gradient only weakly correlated with the catheter peak- to-peak gradient [8]. Both studies confirmed our findings that in most patients peak Doppler echocardiographic gradients correlated only weakly with invasive gradients. However, neither of these studies commented on the additional factors that could have an effect on the gradient estimation.

In a study by Sekar P et al. (2009), 68 patients who underwent Norwood operation were identified retrospectively. Cuff and echocardiographic gradients measured prior to the pre-Glenn catheterization were compared to peak-to- peak systolic neoaortic arch gradients obtained at catheterization. This study found that upper–lower extremity cuff BP gradients do not provide an excellent screening test for clinically important neo aortic arch obstruction in infants with a single ventricle after the Norwood I palliation [13]. In our study there was no difference in the result between single ventricle and biventricular physiology patients.

De Mey S et al. (2001) conducted a study in post surgical coarctation repair patients where Doppler velocities remained elevated due to mild anatomical narrowing secondary to less distensible surgical scar resembling a tubular hypoplasia. They proposed that this allowed an almost complete pressure recovery thus explaining peak Doppler overestimation [16].

To our knowledge, there are no available studies concentrating on the mean Doppler echocardiographic gradients and it's correlation with invasive gradients in children. Although Stout KK et al. used the mean Doppler gradients as a parameter to define significant native or recurrent aortic coarctation in adults [17].

Our data suggests that mean Doppler echocardiographic gradients had the best correlation with invasive gradients. However, cuff blood pressure gradients were accurate only in patients with native COA and infants with weight less than 10 kg. These findings emphasize the value of mean Doppler echocardiographic gradient in estimating coarctation severity. It stresses the importance of four limb blood pressure measurement during clinic follow up visits, especially for infants and those with a native coarctation. Using this knowledge can help to better decide when cardiac catheterization is needed in view of any intervention. These findings could help to better decide on the optimal timing to undergo any catheter based intervention and hence reduce the need for unnecessary diagnostic catheterization.

3.2.3 Limitations of our study:

It's a single center study with a relatively small number of patients. Not all data were available for all patients as this was a retrospective study. The level and type of sedation especially when obtaining the non invasive gradients was not similar in all patients; this could affect the measurement and make the echocardiographic imaging more difficult if the patient is agitated.

4. CONCLUSION

Our study showed that mean Doppler echocardiography is the most accurate among the other noninvasive methods in use to estimate non-invasively severity of aortic coarctation. It provides reasonable agreement with the invasively obtained aortic coarctation gradient. Cuff blood pressure gradients can be used as screening tools in infants. In contrast, the peak instantaneous Doppler pressure gradient is the least reflective of the invasive gradient, and should be less relied on.

Further studies with larger numbers of patients are needed to confirm our findings.

5. ACKNOWLEDGEMENTS

Non

6. COMPETING INTERESTS

Authors have no conflicts of interest to declare.

7. AUTHORS' CONTRIBUTIONS

7.1 Wejdan Khaled Ba-Atiyah : designed the study, collect data, performed the statistical analysis, and wrote the first draft of the manuscript, read and approved the final manuscript.
7.2 Riad Abou Zahr : performed and managed the analyses of the study, read and approved the final manuscript.
7.3 Zaheer Ahmad : read and approved the final manuscript.

7.4 Yahia Mohamed El Mahdi : read and approved the final manuscript.
7.5 Mohammed Omar Galal : designed the study, reviewed the first draft of the manuscript, managed the analyses of the study, read and approved the final manuscript.

8. REFERENCES

1. Seifert BL, DesRochers K, Ta M, et al. Accuracy of Doppler methods for estimating peak-to-peak and peak instantaneous gradients across coarctation of the aorta: An In vitro study. *J Am Soc Echocardiogr.* 1999;12:744-753.

2. Feltes TF, Bacha E, Beekman RH, 3rd, et al. Indications for cardiac catheterization and intervention in pediatric cardiac disease: a scientific statement from the American Heart Association. *Circulation.* 2011;123:2607-2652.

3. Chessa M, Dindar A, Vettukattil JJ, et al. Balloon angioplasty in infants with aortic obstruction after the modified stage I Norwood procedure. *Am Heart J.* 2000;140:227-231.

4. Galal MO, Schmaltz AA, Joufan M, Benson L, Samatou L, Halees Z. Balloon dilation of native aortic coarctation in infancy. *Z Kardiol.* 2003;92:735-741.

5. Shehla Jadoon ME-S, Tarek S. Momenah, M.O. Galal. Percutaneous balloon angioplasty for critical aortic coarctation in newborns and infants: Is it still a valid option? *Journal of the Saudi Heart Association.* 2015;27:303-304.

6. Ali Jelly C, Mohammed Omar Galal, MD, PhD, Fadel Al Fadley, MD, Michael de Moor, MD, Zohair Al Halees, MD. Influence of Associated Defects and Type of Surgery in Neonatal Aortic Coarctation. *Asian Cardiovascular and Thoracic Annals.* 1999;7:115-120.

7. Nihoyannopoulos P, Karas S, Sapsford RN, Hallidie-Smith K, Foale R. Accuracy of two-dimensional echocardiography in the diagnosis of aortic arch obstruction. *J Am Coll Cardiol.* 1987;10:1072-1077.

8. Wisotzkey BL, Hornik CP, Green AS, Barker PC. Comparison of invasive and non-invasive pressure gradients in aortic arch obstruction. *Cardiol Young.* 2015;25:1348-1357.

9. Becker C, Soppa C, Fink U, et al. Spiral CT angiography and 3D reconstruction in patients with aortic coarctation. *Eur Radiol.* 1997;7:1473-1477.

10. F. Zuccarino1 AP, M. C. Escobar-Diaz1, A. Valls1, I. Barber2, J. M. Caffarena1, S. Congiu1, J. Sanchez de Toledo1, J. Munuera1. Advanced cardiovascular computed tomography (CT) imaging in children with congenital heart disease: from volume rendering (VR) to 3D models and 3D printing. *European Society of Radiology* 2020.

11. Giardini A, Tacy TA. Pressure recovery explains doppler overestimation of invasive pressure gradient across segmental vascular stenosis. *Echocardiography.* 2010;27:21-31.

12. Rahiala E, Tikanoja T. Non-invasive blood pressure measurements and aortic blood flow velocity in neonates. *Early Hum Dev.* 1997;49:107-112.

13. Sekar P, Border WL, Kimball TR, et al. Aortic arch recoarctation after the Norwood stage I palliation: the comparative accuracy of blood pressure cuff and echocardiographic Doppler gradients in detecting significant obstruction. *Congenit Heart Dis.* 2009;4:440-447.

14. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986;1:307-310.

15. Christopher AB, Apfel A, Sun T, Kreutzer J, Ezon DS. Diastolic velocity half time is associated with aortic coarctation gradient at catheterization independent of echocardiographic and clinical blood pressure gradients. *Congenit Heart Dis.* 2018;13:713-720.

16. De Mey S, Segers P, Coomans I, Verhaaren H, Verdonck P. Limitations of Doppler echocardiography for the post-operative evaluation of aortic coarctation. *J Biomech.* 2001;34:951-960.

17. Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2019;139:e698-e800.

APPENDIX