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Clinical and Ambulatory Blood Pressure Monitoring in Subjects with Stent Implanted Aortic Coarctation

Stent İmplate Edilmiş Aort Koarktasyonlu Hastalarda Klinik ve Ambulatuar Kan Basıncı İzlemi

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Öz

Giriş ve Amaç: Bu çalışmada başarılı stent implantasyonu yapılmış aort koarktasyonu olan olgularda klinik ve ambulatuvar kan basıncı monitorizasyonu ile devam eden sistemik hipertansiyonu araştırmak amaçlandı.
Gereç ve Yöntemler: Çalışmaya stent implantasyonunun üzerinden en az 6 ay olmak üzere maksimum 3 yıl geçmiş olan aort koarktasyonlu 31 olgu dahil edildi. Olgulara ait demografik, koarktasyonlarına ve stent implantasyonuna ait özellikler, ekokardiyografik bulgular retrospektif olarak incelendi. Çalışma sırasında kan basıncı klasik yöntem ve 24 saatlik ambulatuvar kan basıncı monitorizasyonu ile incelendi. Ekokardiyografileri yapıldı.
Bulgular: Olguların 22'si erkek, 9'u kadındı. Yaş ortalaması 14,50 ± 6,56 yıl idi. Ortalama vücut kitle indeksi 18,61 ± 4,02 bulundu. Olguların 16'sı nativ koarktasyon olgusu iken, diğerleri rekoarktasyon olguları idi. Stent implantasyonu işleminin kan basıncı, ekokardiyografik ve anjiyokardiyografik gradiyentler üzerindeki etkinliği istatistiksel olarak anlamlı bulundu. 11 olgu çalışma sırasında antihipertansif ilaç kullanıyordu. 6 normotansif olguda ambulatuvar kan basıncı izleminde hipertansiyon saptandı. Total bu 17 olgu hipertansif grup, diğerleri normotansif olarak kabul edildi. Hipertansif ve normotansif grup arasında; İşlem öncesi ve sonrası demografik parametreler, koarktasyon tipi ve çapı, stent tipi ve boyutu, ekokardiyografik ve kateter gradiyentlerinde istatistiksel olarak anlamlı fark yoktu.
Sonuç: Optimal tedaviye rağmen, deneklerin önemli bir bölümünde hipertansiyon devam etmekteydi. Bazı normotansif deneklerde ambulatuvar kan basıncı takibi ile hipertansiyon saptandı. Çalışma, klinik kan basıncı izlemenin sadece hipertansiyonu belirlemek için yeterli olmadığını göstermiştir. Stent implante edilmiş aort koarkatsyonlu olgularda kan basıncı takibinde belirli aralıklarla ambulatuvar kan basıncı ölçümü faydalı olacağı saptanmıştır.
Anahtar Kelimeler: Aort koarktasyonu, stent implantasyonu, hipertansiyon, ambulatuvar kan basıncı monitorizasyonu.

Abstract

Objective: This study aimed to investigate the frequency of systemic hypertension by clinical and ambulatory blood pressure monitoring in subjects with stent implanted aortic coarctation.
Materials and Methods: The study included in 31 subjects with stent implanted aortic coarctation before at least 6 months to 3 years. Related features of subjectes, procedure, echocardiografhic findings were evaluated retrospectively. Blood pressure were examined by classical method and 24-hour ambulatory blood pressure monitoring.
Results: 22 of subjects were male and 9 were female. Mean age was 14.50 ±6.56 years. The mean body mass index was found to be 18.61 ±4,02.16 of them had native coarctation, others had recoarctation. The efficiency of procedure on blood pressure, echocardiographic and angiocardiographic gradients was found to be statistically significant. 11 subjects were using antihypertensive drug. Six normotensive subjects had hypertensive in ambulatory blood pressure monitoring.17 subject were considered hypertensive group, others normotensive. There was not statistically

significant difference between hypertensive group and normotensive group in demographic paramaters, coarctation type and diameter, the stent type and size, echocardiographic and catheter gradients before and after the procedure.
Conclusion: Despite optimal treatment, hypertension persists in an important part of the subjects. Some normotensive subjects had hypertensive with ambulatory blood pressure monitoring. The study showed that clinical blood pressure monitoring does not sufficient to determined hypertension alone. Ambulatory blood pressure measurement with regular intervals will be beneficial in the follow-up of these subjects for hypertension.
Key Words: Aortic coarctation, stent implantation, hypertension, ambulatory blood pressure monitoring.

1. Introduction

Aortic coarctation is obstruction in any part of the descendent aorta generally at a point distal to the left subclavian artery. [1-4] Although The simplicity of its anatomical appearance, It is a rather complex pathology in terms of its clinical presentation, treatment options and long-term prognosis.

Crafoord and Nylin performed the first successful surgical treatment of coarctation in 1944 [2-4, 6], then balloon angioplasty (1982) and stent implantation (1991) were added.[1-4]. Despite all these different treatment options, the efficiency of these treatments in eliminating coarctation, the long-term prognosis of the disease is not benign.[5] Systemic hypertension is one of the most important factors which worsens the prognosis.

Despite successful coarctation treatment it is known that hypertension at rest, hypertension during daily acitivities and/or exercise-induced hypertension persists in many cases.[7,8] The cause of hypertension in patients with coarctation has not been fully elucidated. Factors including residual coarctation, scar tissue, graft interposition, increased aortic stiffness, decreased compliance, disrupted arterial reactivity, abnormal pulsed wave velocity, decreased baroreceptor reflex function and disrupted anatomy of the aortic arch have been implicated.[7,8]

In this study we aimed to investigate the frequency of hypertension with clinical examination (arterial blood pressure measurement) and additionally with ambulatory blood pressure monitoring in subjects with stent implented aortic coarctation who had no rezidual or recurrent coarctation.

2. Material ve Metods

The study included in 31 subjects with stent implanted aortic coarctation. The stent implantation procedure had performed at least 6 months to 3 years in all subject. İn pediatric Cardiology policlinic, the subjects was included who regularly follow-up stent implented aortic coarctation and who gave consent for the study. The study group was composed of children above 5 years of age, adolescents and adults. Retrospective evaluation of the demographic characteristics, features related to stent implantation procedure, examination findings and echocardiography findings before procedure was examined retrospectively.

Stent implantation was performed successful and optimal for all patients. After the procedure the subjects were followed up regularly by echocardiography and blood pressure measurements in all four extremities at 1, 3, 6 and 12 months. The antihypertensive drugs used were learned from follow-up records, from the subjects themselves or from the families.

At the study time, after general physical examination and a 5-minutes rest, blood pressure measurements were done in all four extremities seperately 3 times using Marquette Type 555 (Hellige Medical Systems) Doppler blood pressure monitor in the supine position. The study was based on the mean value of the measurements. The difference between the systolic blood pressures measured in the right arm and right leg was recorded. Blood pressure values were classified accoring to age, gender and height percentile tables stated in the 4th report of National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. A value of 95th percentile and above was considered to be hypertension.[10] The study was performed without discontinuing the antihypertensive drugs used by the subjects to eliminate the disadvantages.

Echocardiography at baseline and in follow-up vizits was performed using (Vivid 3 Pro, GE Medical Systems, Vingmed Ultrasound AS, N-3190 Horten, Norway). Coarctation region in the descendent aorta and gradients in the stent region were recorded by Doppler. Additional abnormalities accompanying coarctation were determined by echocardiography.

A one-day Holter monitoring was performed in the subjects using an ambulatory blood pressure Holter device (Tracker NİBP2, Del Mar Reynolds Medical) .The cuff was placed on the right arms of the subjects. The subjects were told to continue their daily acitivities during the procedure avoiding intense effort. The obtained ambulatory blood pressure values were evaluated according to the normal values of ambulatory blood pressure in healthy white children reported by Wühl et al.[11] Subjects who were found to have a value above the 95th percentile were considered as the hypertensive group, others as the normotensive group. The subjects who were diagnosed clinically as hypertension and who were receiving antihypertensive treatment were considered in the hypertensive group. Consent was obtained from the local ethics committee, from the adult patients and from the families of pediatric patients for the study.

Analysis of the data was done using SPSS 16 (Statistical Package of the Social Sciences, SPSS Inc. Chicago, Illinois) statistical package program. A p less than 0.05 was considered statistically significant in all analyses.

3. Results

21 (71%) of 31 subjects were male and 9 (29%) were female. At the time of the study, the mean age of the

subjects was found to be 14,50 ±6,56 (5-37, median:13,48) and the mean body mass index was found to be 18,61 ±4,02 (12,84-25,71, median 17,51). 16 (51,6%) of the subjects had native coarctation and 15 (48,4%) had recoarctation. 11 (35,5%) of these 15 subjects had recoarctation after balloon and 4 (12,9%) had recoarctation after surgery. 28 (90,3%) of the subjects had discrete lesion and 3 (9,7%) had tubular lesion. (Table 1).

Bare-metal stent was used in 23 subjects and covered stent was used in 8 subjects. The optimal criterion for success was considered as a "peak to peak" systolic pressure gradient lower than 10 mmHg after stent implentation. Echocardiographic and catheter coarctation gradient before and after stent implantation was showed at Table 2.

Table1. Characteristics of coarctation in all patients in the study group

Manifestations		Number	%
Characteristic of coarctation	Native	16	51,6
	Recoarctation after balloon	11	35,5
	Recoarctation after surgery	4	12,9
Morphology of coarctation	Discrete	28	90,3
	Tubular	3	9,7
Characteristic	Isthmus hypoplasia	1	3,1
	Association of patent ductus arteriosus	3	9,4
	Subatretic	2	6,2

Table 2. Comparison of ascendent aorta and descendent systolic pressures gradients obtained from echocardiography and catheter before and after stent implantation

Pressures and gradients (mmHg)	Before the procedure (n:31)	After the procedure (n:31)	t*	p**
Echocardiographic gradient	59,4 ±16,9	28,3 ±12,0	8,53	0,00001
Ascendent aorta sysytolic blood Pressure	151,1 ±20,5	136,9 ±15,2	3.73	0,001
Ascendent aorta diastolic blood Pressure	73,4 ±22,2	64,4 ±15,0	2,31	0,0275
Ascendent aorta-descendent aorta pressure gradient	42,4 ±15,9	2,9 ±3,6	14,57	0,00001

* Paired sample t test, ** p <0.05 significant

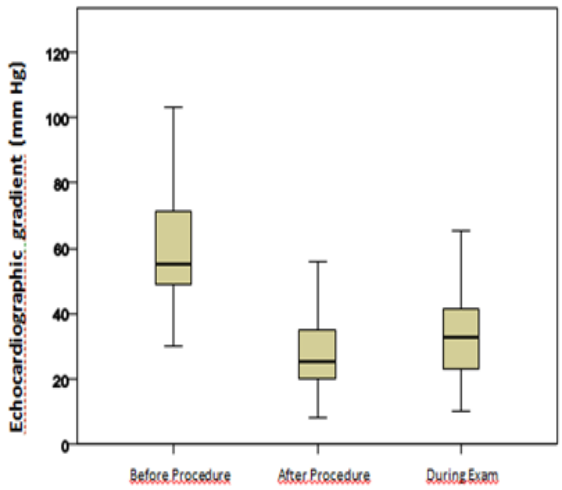

Figure 1. The pressures difference between peak –to-peak gradient with CW Doppler in coarctation region obtained by echocardiography of 31 stent-implanted subjects are shown at first box diagram, one day after stent implantation at second box diagram and during the study at third box diagram at the figure.

The echocardiography coarctation gradients on the first day, at the first month and 6th month after stent implantation was observed that a significant decrease compared to the values measured before precedure, but no significant increase occured in terms of gradient in the follow-up (Figure 1).

While the mean echocardiographic gradient before the procedure was found to be 59,4 ±16,9 mm Hg (30-103, median 55 mm Hg), this value decreased to 28,3 ±12,0 (8-40, median 25 mm Hg) mm Hg after the procedure (p: 0,0001) (Figure 1). However, although echocardiographic gradient increased to 32,4 ±13 (10-45, median 32 mm Hg) mm Hg during the study, this was not found to be statistically significant (p: 0.052). In addition, typical diastolic flow pattern specific for coarctation could not be obtained in any subject. Therefore, systemic hypertension which can be found in these subjects is not related to residual or recurrent coarctation.

Upper and lower extremity arterial pressures obtained noninvasively with a blood pressure monitor before stent implantation and one day after stent implantation and comparison of their differences are summarized in Table 3.

Table 3. Comparison of upper-lower extremity arterial pressures measured non-invasively with a blood pressure monitor before and after stent implantation and their differences

Pressures and gradients (mmHg)	Before the procedure (n:31)	After the procedure (n:31)	t*	p**
Right arm systolic blood pressure	136,2 ±18,0	125,2 ±17,0	3,38	0,0020
Right arm diastolic blood pressure	73,4 ±22,2	64, ±415,0	2,31	0,0275
Difference between upper and lower extremity systolic pressures	35,6 ±20,1	6,7 ±16,4	6,89	<0,00001

***** *Paired sample t test,* ****** *p <0.05 significant*

Mean right arm systolic blood pressure measured after stent implantation decreased significantly (p: 0,0020). This result shows that stent implantation procedure has a positive effect on systolic blood pressure. The right arm diastolic blood pressure showed a statistically significant difference between the value before stent implantation and the value after stent implantation (p: 0,0275). The mean difference between the upper and lower extremity systolic blood pressures was also found to be statistically significant to a considerable extent (p: 0,00001).

The subjects were evaluated clinically with manuel and ambulatory blood pressure monitoring after a mean period of 14.2 ±9.1 (6-30, mediyan 13,6) months after procedure.

11 of 31 subjects who were included in the study were using antihypertensive drug. Nine subjects were using beta-blocker, one subject was using angiotensin converting emzyme inhibitor and one subject was using beta blocker and angiotensing converting enzyme inhibitor.

It was observed that blood pressures in three who were using antihypertensive drugs were completely under control in the clinical follow-up and ambulatory Holter monitoring.

Five subjects had hypertensive ambulatory Holter values and three subjects had prehypertensive values (90-95th percentile). Despite the antihypertensive treatment, the blood pressure of these subjects were uncontrolled.

With clinical arterial blood pressure measurements, hypertension was found in 5 of 20 subjects who were not using antihypertensive drugs. In three, hypertension was also found with ambulatory blood pressure measurements. the other 2 subjects were normal in ambulatory blood pressure measurements, they were considered to have white coat hypertension.

Again, three subjects were found to be hypertensive with Holter monitoring, although their clinical systolic blood pressure measurements were found to be within normal limits. These were considered as masked hypertension. Thus, the actual frequency of hypertension was 6 of 20 among the subjects who were not using antihypertensive drugs. Four prehypertensive subjects with normal clinical systolic blood pressure values and non-hypertensive values in Holter monitoring which needed close follow-up (90-95th percentile) were found in this group.

Parametric and nonparametric values were compared between 14 normotensive subjects and 17 hypertensive subjects. (Table 4).

No statistically significant difference was found between the two grups in terms of age, weight, body mass index, coarctation diameter, echocardiographic and angiocardiografic gradient before and after the procedure, stent lentghs used (p <0.05).

Again, no statistically significant difference was found between the two grups in terms of gender, coarctation type (native, recoarctation), stent type used (covered, bared), age at the time of first intervention below or above 10 years. (p above than 0,05).

4. Discussion

Aortic coarctation constitutes 4-8% of congenital cardiac diseases [1-4]. Life expectancy was found to be decreased in patients with aortic coarctation who had been treated compared to healthy normal adults [1-4,12-14].

The main problems observed in these patients include recoarctation, aortic aneurism or aortic dissection, biküspid related complications, endocarditis, early coronary atherosclerosis, cerebrovascular events and systemic hypertension.

Table 4. Comparison of parametric characteristics of normotensive and hypertensive subjects

	Subjects by Blood Pressure Status			
	Normotensive (n:14)	Hypertensive (n:17)	t	p
Body mass index	17,8 ±4,049	19,28 ±4,01	-1,01	0,321
Weight (kg)	43,32 ±19,69	48,9 ±119,06	-0,80	0,430
Height (meter)	1,51 ±0,22	1,5 ±50,21	-0,51	0,613
The age at the first procedure (years)	11,54 ±9,27	10,11 ±5,59	0,51	0,609
Echocardiographic gradient before the procedure (mmHg)	59,00 ±19,93	60,94 ±14,11	-0,31	0,754
Catheter gradient before the procedure (mmHg)	43,00 ±14,33	43,35 ±16,44	-0,06	0,950
Catheter gradient after the procedure (mmHg)	2,00 ±2,88	3,4 ±13,89	-1,12	0,269
Ascendent aorta systolic blood pressure before the procedure (mmHg)	148,50 ±19,46	152,7 ±620,59	-0,58	0,561
Ascendent aorta systolic blood pressure after the procedure (mmHg)	134,79 ±15,90	137,59 ±14,30	-0,51	0,610
Stent lenght (mmHg)	31,57 ±6,89	35,24 ±8,72	-1,27	0,212
Coarctation diameter (mmHg)	6,39 ±3,08	7,68 ±2,91	-1,20	0,240

Persistent systemic hypertension is the major factor contributing to increase in the cardiovascular risk and is found in 17-57% of the patients who have been treated for coarctation. [7,9]

The effects of surgical treatment, balloon angioplasty and stent implantation performed for treatment of aortic coarctation on hypertension and in cases of exercise hypertension have been the subject of many studies and investigated with various aspects [9,15-30].

Harrison et al. reported systemic hypertension regressed in 19 of 26 subjects in whom stent implantation was performed and Magee et al reported the need for drug treatment was eliminated in 9 of 17 subjects after stent implantation [32,33] Carr complied and compared the articles related to invasive and surgical treatments in 2006 [34]. In these studies, it was found that the mean rate of hypertension was 61% (18-88%) in the invasive group and 64% (13-76%) in the surgery group. Thus, the rate of hypertension was found to be similar in these groups [34].

The effects of stent implantation in lowering arterial blood pressure have been discussed in many aspects in different studies. Hamdan et al. found that the systolic blood pressure decreased from 136 ±21 mm Hg to 122 ±19 mm Hg in 31 subjects with coarctation (13 of them were native) with a mean age of 16 in whom they performed stent implantation in 2001.[35] While hypertension was present in 71% of these subjects and a history of drug usage was present in 42% before the procedure, hypertension and drug usage persisted in only 26% after the procedure [35]. Tzifa et al. reported antihypertensive treatment was discontinued or the drug dose was decreased in the follow-up after the procedure in 43% of 33 subjects with a mean age of 28 (8-65 years) in whom they performed covered stent implantation.[36]

Musto et al. followed up 21 subjects with an age of 12-73 years in whom 8 balloon angioplasty and 13 stent implantation were performed for a mean period of 50,6 months (6-82 months) in the study they performed in 2008. They demostrated the effect of invasive interventions in lowering blood pressure by finding that the systolic blood pressure decreased from 157 ±16 mmHg to 123 ±13mm Hg after the first month in the follow-up in these subjects.[37] However, they observed that hypertension persisted in 33% of the subjects in the follow-up.[37]

When we examined the echocardiographic and angiocardiographic gradient values in our study group before the procedure, after the procedure and during the study, we observed that the interventions were successful. When the right arm systolic and diastolic blood pressure values and the difference between the right arm-right leg blood pressure were examined before the procedure, after the procedure and during the study, the efficiency of the interventions performed was demostrated.

In our study, it was observed that 17 (54,8%) of 31 subjects were hypertensive and 14 (45,2%) were normotensive. Although this rate seems to be high, it is compatible with the findings in the literature. [7,8,14,38] There was a significant difference between normotensive and hypertensive group in terms of mean systolic blood

pressure, nocturnal and daytime systolic blood pressure and systolic blood pressure load. However, there was no statistically significant difference between these two groups in terms of age, gender, body weight and body mass index, coarctation type (native or recoarctation) and stent type used. Again, there was no statistically significant difference between these two groups in terms of coarctation diameter, echocardiographic and catheter gradients before and after the procedure, ascendent aorta pressures before and after the procedure and stent lenght used ($p < 0,05$).

It is considered that a diagnosis of hypertension based on ambulatory blood pressure measurements in adults and children gives more valuable results compared to clinical blood pressure measurement.[39-46] In our study, white coat hypertension was found in 2 (6,5 %) of 31 subjects. Ambulatory blood pressure monitoring is reported to be the most reliable method to differentiate white coat hypertension from actual hypertension. [47,48] Observation of white coat hypertension also in our study suggests that ambulatory blood pressure monitoring may be appropriate in the diagnosis and follow-up of aortic coarctation cases to avoid unnecessary antihypertensive drug usage. [47,48]

On the other hand, diagnosing masked hypertension cases is important, since these individuals have been reported to have an equal risk as individuals with persistent hypertension in different studies.[47,48] In our study, masked hypertension was found in 3 (9,7 %) of 31 subjects. Because of the possibility of skipping masked hypertension with only clinical measurement, ambulatory blood pressure measurement in these subjects is important.[47,48]

Another finding of us which showed the importance of ambulatory blood pressure measurement was the fact that 5 subjects still had hypertensive blood pressure values in ambulatory blood pressure Holter monitoring, although they were using antihypertensive drugs. 3 subjects who were using antihypertensive drugs had prehypertensive values (between the 90th and 95th percentiles of blood pressure measurement) in ambulatory Holter monitoring. The relation between prehypertension and persistent hypertension was examined in various studies and the importance of follow-up in these subjects was emphasized.[39] Considering the risk of conversion of prehypertension to persistent hypertension in the follow-up, long-term follow-up of these subjects and examination in terms of end-organ demage are important.[39]

While 20 of 31 subjects in our study group were not using antihypertensive medication, 14 of 20 subjects who had normotensive findings in ambulatory, others had not. 5 of 11 subjects in the hypertensive drug using group were hypertensive at ambulatory blood pressure measurement, despite therapy. After diagnosing hypertension with ambulatory blood pressure measurement, it was revised drug therapy.

The cause of the recurrence of hypertension in cases with treated coarctation is unknown. It is thought that administering treatment at an early age helps prevent hypertension based on the observation that the rate of hypertension in cases that were surgically treated before the age of 1 was 10%, while the rate was 33% on those that were treated after the age of 14 (13). However, although hypertension can be prevented with treatment, it was observed that it recurred during the follow-up of the patients (14), which may have been caused by the late administration of treatment and native coarctation, which was observed in 16 of the patients (51%) in our study group. Potential causes of post-treatment hypertension are thought to be hyper activation of the renin-angiotensin system, baroreflex failure, reactivity dysfunctions of the arteries, which include the increase in resistance of small arteries, the decrease in reactivity of medium-large arteries and the functional and structural damage that leads to increased stiffness in the arteries (7). There are different perspectives on the impact of hyper activation of the renin-angiotensin system and baroreflex failure on the recurrence of hypertension in such cases. Regarding vascular reactivity dysfunction, it was observed that although the arteries recovered their elasticity after the coarctation treatment, vascular reactivity dysfunction continued, indicating that it starts at an early age and does not respond to treatment (7), suggesting that it might be a cause of recurring hypertension. However, further research on the cause of recurring hypertension post-coarctation treatment is required for a better understanding of the condition.

5. Conclusion

Stent implantation is an efficient method in treatment of coarctation. With this treatment systolic and diastolic arterial blood pressures decrease significantly and systemic hypertension is affected positively. However, hypertension persists in some of the patients even though sufficient dilatation and optimal decrease in gradients. In some of these subjects, hypertension can not be demostrated with classical measurements and can only diagnosed in ambulatory blood pressure monitoring.

It is not possible to predict which subjects will have persistent hypertension after interventional treatment. Therefore, close clinical follow-up is necessary after intervention. In addition to standard arterial blood pressure measurement, ambulatory blood pressure monitoring should be performed and repeated periodically. In this way, the diagnoses of prehypertension, masked hypertension and white coat hyperension can be made accurately. Ambulatory blood pressure monitoring is also important for evaluation of the efficiency of antihypertensive drug treatment and for tailoring treatment.

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