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Do We Apply Guidelines During Our Daily Practice in Coronary Revascularization?

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Abstract

Myocardial revascularization guidelines help cardiologist and cardiovascular surgeons to determine the best treatment option for revascularization of the diseased coronary arteries. However, in daily practice compliance to guidelines are generally insufficient. Cardiologist might prefer ad hoc coronary stent implantation without discussing the patients with the surgeons. Creating a "heart team" and activating it, during the decision-making period is recommended in the guidelines. In addition, the importance of patient participation is emphasized in determining the treatment strategy. In this article we aimed to investigate the compliance of the cardiologist and cardiovascular surgeons to the guidelines, and to determine the factors that interfere with the application in daily practice.

Keywords: Coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention

Introduction

In patients with coronary artery disease, coronary revascularization improves symptoms, survival and quality of the life. Coronary revascularization might be performed in two ways: Coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). Although both have been proven to be effective and safe, there are still great variations in clinical practice. Guidelines have been developed in clinical practice to solve confusion and determine the most appropriate treatment for the patient[1]. However, compliance with guidelines has not been reached the desired level in daily clinical practice.

Guidelines on myocardial revascularization are constituted by Cardiologist and cardiovascular surgeons together with meticulous work. Latest ESC/EACTS

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guidelines related to myocardial revascularization which was published in 2018, was prepared using 786 references(2). In order to constitute the current Guidelines, Task Force performed a systematic review of all randomized controlled trials performed since 1980, comparing different revascularization strategies and retrieved at least 100 RCTs involving almost 90,000 patients(2).

Guidelines help health care professionals to individualize their decision for all patients. However, patients should play active role in the decision-making process about the treatment strategy, especially in the presence of the conflict among different treatment options (Table 1). During determination of the treatment strategy, not only the results of the studies and the physician's evaluation, but also the active participation of the patient results in better outcomes(2).

In routine daily practice mostly, cardiologists decide for PCI during the coronary angiography. Cardiologists consult the patient to a surgeon if the patient is not suitable for single stage procedure. Also, consultant cardiovascular surgeon decides and gives information about the process

Table 1. Recommendation for decision making process(2)

Recommendation	Class[a]	Level[b]
It is recommended that patients undergoing coronary angiography are informed about benefits and risks, as well as potential therapeutic consequences, ahead of the procedure	I	C
It is recommended that patients are adequately informed about short- and long-term benefits and risks of the revascularization procedure with information about local experience and allowed enough time for informed decision-making	I	C
It is recommended that institutional protocols are developed by the Heart Team to implement the appropriate revascularization strategy in accordance with current Guidelines	I	C
In PCI centres without on-site surgery, it is recommended that institutional protocols are established with partner institutions providing cardiac surgery	I	C

[a]Class of recommendation, [b]Level of evidence, PCI: Percutaneous coronary intervention

to the patients who are candidates for surgery, instead of council decision. In stable complex coronary artery diseases, multidisciplinary decision-making has become more important in determining optimal treatment strategy. However, it is still not widely used. As a result, there are variations in the PCI/CABG application rates due to physician-related factors. Daily practice is changed due to increasing concerns about treatment practices that are not in accordance with the established criteria.

In this article, it is aimed to emphasize the importance of the council in which the patient is involved in decision making process by drawing attention to the applications in real life.

Results

Guidelines have three basic features in general: They address almost all clinical scenarios that a clinician may encounter; importance of multidisciplinary approach of the heart team; importance of patients' information(3). Collaboration of the patient and health professionals is important to cope up with the complications after the procedure. However, it was found that, in the patients undergoing PCI and CABG alternative therapies were not discussed in 70% of PCI patients, and in 60% of CABG patients(4).

Hannan et al.(5) investigated the impact of evidence-based guidelines on referral decisions in daily practice with evaluating a total of 16,000 patients who had undergone catheterization in hospitals of New York. Of the patients who were indicated for CABG, only 53% were recommended for CABG and 34% were recommended for PCI. Otherwise, of the patients indicated for PCI, 94% were recommended for PCI. Patients who were indicated for both CABG surgery and PCI, 93% were recommended for PCI and only 5% for CABG (Table 2).

Drug eluting stents encouraged cardiologists to perform PCI in the patients with Class I indication for CABG(6). Currently, the rates of CABG and PCI applications have been varied considerably due to physican-related factors. A significant number of patients do not receive treatment on the basis of common consensus guideline. This is sometimes an obstacle for patients to receive the optimum treatment. Most appropriate way to cope up with this problem is to do final decision with discussion by cardiologists and surgeons "Heart Team", and taking the opinion of patients especially for the complex disease. In this century, patients can easily reach information about their disease from the internet and media. This increases patient expectations and they want to be informed about all treatment options. Transparency about the treatment options and cooperation with the patient will improve patient's satisfaction during the treatment period[7].

Performing therapeutic intervention in the same procedure with diagnostic angiography is named as ad hoc. Patient might be treated at single stage with decreased complication rates related to the second procedure. Patient with LMCA or proximal LAD and three vessel disease should be discussed by the heart team instead of ad hoc PCI[2]. In the evaluation of more than 45,000 patients, revascularization rates and mortality in 3 years were significantly higher in ad hoc procedure[8]. Also, it was revealed that 30% of patients who were candidates for CABG referred to ad hoc procedure[2,8].

Desai et al.[9] evaluated the patients who had undergone PCI or CABG and their optimal treatment recommendation according to the ACC/AHA guidelines. While 90% of the patients who had undergone CABG were appropriate for revascularization, this rate was 36% for PCI. It was found that 14% of the patients with PCI were inappropriate, and 50% were uncertain according to the guidelines.

After determining Appropriate Use Criteria in 2009, inappropriate intervention rate of non-acute PCI was decreased from 26% to 13%. However, inappropriate PCI still persists in different levels (from 5.9% to 23%) in different hospitals[10]. It was revealed that physicians do not mention alternative treatment options in 59% of CABG patients and 68% of PCI patients[4]. In contrast, 4,684 patients who had undergone CABG was evaluated and it was found that 98.6 (87.7% Class I and 10.9% Class II) of the operations were appropriate[11].

In the guidelines, development of the "heart team" protocol and discussing the benefits and risks of the revascularization procedures are recommended as Class 1 indication[2]. The member of the heart team should include at least one cardiac surgeon, one interventional, and one non-interventional cardiologist[12]. The "heart team" application has emerged to determine the optimal treatment strategy for patients with stable complex coronary artery disease. However, in daily practice "Heart Team" concept is not widespread due to physician-related factors. Approach to the patients with stable, complex coronary artery disease varies between the countries. While PCI/CABG ratio was 0.67 in Mexico, it was increased to 8.63 in Spain. Even within the same health care system, a large difference in PCI-to-CABG ratios has been reported across different regions[13]. As a member of the heart team, cardiologist should be in cooperation with cardiovascular surgeon for decision making based on the guidelines[3].

In the comparison of CABG and PCI for 5 years follow up of the SYNTAX trial; myocardial infarction

Table 2. Comparison of revascularization procedure and ACC / AHA indications vs catheterization recommendation[5]

ACC / AHA indications vs catheterization recommendation	CABG, n (%)	PCI, n (%)	Medical treatment, n (%)	None, n (%)	Total, n (%)
CABG	712 (53)	455 (34)	156 (12)	14 (1)	1337 (100)
PCI	124 (2)	5660 (94)	255 (4)	12 (<1)	6051 (100)
CABG and PCI	84 (5)	1608 (93)	26 (2)	4 (<1)	1722 (100)
Neither CABG or PCI	70 (6)	261 (21)	873 (71)	19 (2)	1223 (100)
Total	990 (10)	7984 (77)	1310 (13)	49 (<1)	10,333 (100)

CABG: Coronary artery bypass grafting, PCI: Percutaneous intervention, ACC: American College of Cardiology, AHA: American Hospital Association

(3.8% vs 9.7%) repeat revascularization (13.7% vs 25.9%), all-cause mortality (11.4% vs 13.9%) were significantly high in PCI patients. While MACCE scores were similar in the patients with low SYNTAX score, MACCE score was significantly high with PCI in the patients with intermediate and high scores[14]. In 3-vessel disease and/or left main coronary patients, CABG has superiority to PCI with lower rates of death, myocardial infarction and repeat revascularization. CABG is still best treatment option in 71% patients according to the five-year results of SYNTAX[15]. Similarly, in the comparison of the 3 years follow up of the everolimus-eluting stents and CABG, although mortality rates were similar, myocardial infarction and repeat revascularization rates remained higher in PCI group[16]. CABG should be the gold standard for the coronary revascularization. PCI might be an alternative in the patients with low SYNTAX scores[14].

Recent guidelines recommend approach to the CAD with the guidance of SYNTAX score (Table 3). Clinical condition of the patients, comorbidities and confounding factors such as diabetes should be evaluated by the heart team in the decision process[10].

Conclusion

Currently, more or less than necessary and improper myocardial revascularization is still frequently encountered and significant differences are observed between different geographic regions and hospitals. Underuse of revascularization when it is necessitated increases mortality[16]. Performing optimal technique is important to improve postoperative outcomes. It is obvious that the wide variations of the interventions are related to the physician and this will be turned into a necessity for reimbursement by a health system (state and private) in the near future. In other words, it will be attempted to ensure that the practices are patient-based rather than physician-based[11].

A well-balanced multidisciplinary "Heart Team" consisting of clinical cardiologist, interventional cardiologist and cardiac surgeon helps to better interpret the data, to apply appropriate treatment according to the guidelines and to make a more objective and uniform decision by considering the experiences and patient preferences[17,18]. In our hospital we discussed the gray zone patients by the heart team with the patients' clinical

Table 3. Recommendation for revascularization procedure[2]

Disease	CABG		PCI	
	Class[a]	Level[b]	Class[a]	Level[b]
One vessel CAD				
With proximal LAD stenosis	I	A	I	A
Two vessel CAD				
With proximal LAD stenosis	I	B	I	C
Left main CAD				
Left main disease with low SYNTAX score (0-22)	I	A	I	A
Left main disease with intermediate SYNTAX score (23-32)	I	A	IIa	A
Left main disease with high SYNTAX score (>33)	I	A	III	A
Three-vessel CAD without diabetes mellitus				
Three-vessel disease with low SYNTAX score (0-22)	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score (>22)	I	A	III	A
Three-vessel CAD with diabetes mellitus				
Three-vessel disease with low SYNTAX score (0-22)	I	A	IIb	A
Three-vessel disease with intermediate or high SYNTAX score (>22)	I	A	III	A

[a]Class of recommendation, [b]Level of evidence, PCI: Percutaneous coronary intervention, LAD: Left anterior descending, CAD: Coronary artery disease

status and angiographic findings. Then we decided our approach after informing the patients about advantages and disadvantages of the both procedures.

The physicians are responsible for taking the patient's and their relatives' opinions on the basis of the scientific data and for implementation of the most appropriate and correct treatment. It is necessary to decide the intervention, base on the guidelines prepared by keeping all randomized controlled trials. In cases where more than one treatment option may be valid, the final decision must be given by the "Heart Team", which is composed of the surgeon and cardiologists. Involvement of the patients in the decision-making process is important in order to start the treatment process as a team with the patient. Also, it is important to protect the health professionals from legal problems when complications are developed.

Ethics

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Authorship Contributions

Surgical and Medical Practices: E.D., Concept: E.D., Design: E.D., Data Collection or Processing: İ.D., M.U., Analysis or Interpretation: E.D., İ.D., M.U., Literature Search: İ.D., M.U., Writing: E.D., İ.D., M.U.

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References

1. Yates MT, Soppa GK, Valencia O, et al. Impact of European Society of Cardiology and European Association for Cardiothoracic Surgery Guidelines on Myocardial Revascularization on the activity of percutaneous coronary intervention and coronary artery bypass graft surgery for stable coronary artery disease. J Thorac Cardiovasc Surg 2014;147:606-10.
2. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;55:87-165.
3. Ribichini F, Taggart D. Implications of new ESC/EACTS guidelines on myocardial revascularization for patients with multivessel coronary artery disease. Interact Cardiovasc Thorac Surg 2011;12:663-6.
4. Chandrasekharan DP, Taggart DP. Informed consent for interventions in stable coronary artery disease: problems, etiologies, and solutions. Eur J Cardiothorac Surg 2011;39:912-7.
5. Hannan EL, Racz MJ, Gold J, et al. Adherence of catheterization laboratory cardiologists to American College of Cardiology/American Heart Association guidelines for percutaneous coronary interventions and coronary artery bypass graft surgery: what happens in actual practice? Circulation 2010;121:267-75.
6. Head SJ, Kaul S, Mack MJ, et al. The rationale for Heart Team decision-making for patients with stable, complex coronary artery disease. Eur Heart J 2013;34:2510-8.
7. Hannan EL, Samadashvili Z, Walford G, et al. Predictors and outcomes of ad hoc versus non-ad hoc percutaneous coronary interventions. JACC Cardiovasc Interv 2009;2:350-6.
8. Hannan EL, Cozzens K, Samadashvili Z, et al. Appropriateness of coronary revascularization for patients without acute coronary syndromes. J Am Coll Cardiol 2012;59:1870-6.
9. Desai NR, Bradley SM, Parzynski CS, et al. Appropriate use criteria for coronary revascularization and trends in utilization, patient selection, and appropriateness of percutaneous coronary intervention. JAMA 2015;314:2045-53.
10. Head SJ, Davierwala PM, Serruys PW, et al. Coronary artery bypass grafting vs. percutaneous coronary intervention for patients with three-vessel disease: Final five-year follow-up of the SYNTAX trial. Eur Heart J 2014;35:2821-30.
11. Holmes DR Jr, Rich JB, Zoghbi WA, et al. The heart team of cardiovascular care. J Am Coll Cardiol 2013;61:903-7.
12. Mishra PK, Luckraz H, Aktuerk D, et al. How does the 'Heart Team' decision get enacted for patients with coronary artery disease? Heart Asia 2014;6:31-3.
13. Bangalore S, Guo Y, Samadashvili Z, et al. Everolimus Eluting Stents Versus Coronary Artery Bypass Graft Surgery for Patients With Diabetes Mellitus and Multivessel Disease. Circ Cardiovasc Interv 2015;8:e002626.
14. Luckraz H, Norell M, Buch M, et al. Structure and functioning of a multidisciplinary 'HeartTeam for patients with coronary artery disease: Rationale and recommendations from a joint BCS/BCIS/SCTS working group. Eur J Cardiothorac Surg 2015;48:524-9.
15. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel diseaseabd left main coronary disease. 5-year follow-up of the randomized, clinical SYNTAX trial. Lancet 2013;38:629-38.
16. Filardo G, Maggioni AP, Mura G, et al. The consequences of under-use of coronary revascularization; results of a cohort study in Northern Italy. Eur Heart J 2001;22:654-62.
17. Frutkin AD, Lindsey JB, Mehta SK, et al. Drug-eluting stents and the use of percutaneous coronary intervention among patients with classI indications for coronary artery bypass surgery undergoing index revascularization: analysis from the NCDR (National Cardiovascular Data Registry). JACC Cardiovasc Interv 2009;2:614-21.
18. Long J, Luckraz H, Thekkudan J, et al. Heart team discussion in managing patients with coronary artery disease: outcome and reproducibility. Interact Cardiovasc Thorac Surg 2012;14:594-8.

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How Can We Treat Asymptomatic Carotid Disease in Patients with a Planned CABG?

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Abstract

Carotid artery intervention to the neurological asymptomatic patients is one of the most controversial issues of vascular surgery throughout the last decades. The decision about how to manage asymptomatic carotid disease in the setting of planned coronary artery bypass graft (CABG) becomes more complex due to surgical treatment of either pathology may be complicated by multiple factors. Current guidelines do not support routine screening for carotid artery stenosis before CABG because of given the low prevalence of stroke after CABG. Optimal surgical intervention and timing for patients having concomitant severe carotid and coronary artery stenosis remains uncertain. In this brief review, we analyze the incidence of significant carotid stenosis in patients undergoing CABG, association of untreated asymptomatic carotid stenosis on postoperative stroke, effects of carotid endarterectomy (CEA) on postoperative incidence of stroke, determination of surgical options and technical variations for CEA, scanning methods for identifying the vulnerable carotid plaque and revealing risk factors and predictors associated with stroke after CABG. Synchronous or staged CEA still remain valuable options in order to diminish postoperative risk of stroke for neurologically asymptomatic patients undergoing to CABG who have bilateral significant carotid artery stenosis or contralateral occlusion.

Keywords: Carotid endarterectomy, carotid stenosis, coronary artery bypass, stroke

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Introduction

Stroke is the most dreadful complication of all cardiac surgery procedures and remains an important cause of mortality and permanent disability. In Europe, stroke is responsible for 1.1 million deaths each year, making it second commonest cause of death and more than half of all stroke survivors remain dependent on others for daily activities[1]. Following the introduction of carotid endarterectomy (CEA) in 1954 for the prevention of stroke in symptomatic patients, an increasing proportion of carotid interventions were undertaken in neurologically symptomatic patients[2]. Uncertainty about the ideal treatment of these patients makes it essential for us to understand about the causes of stroke. Usually, all our attention were directed on carotid disease as being a key source of stroke but forgetting that there are many other important causes as well. The mechanisms underlying development of post-operative stroke are multiple and mostly of cardiac origin as thromboembolism may occur from left sided heart chambers and ascending aorta[3]. Patients with severe carotid artery stenosis undergoing coronary artery bypass graft (CABG) face a higher risk of stroke than patients without carotid disease but most strokes are unrelated to carotid disease[4,5]. Although several strategies have been developed for minimize to peri-operative stroke such as avoiding the manipulation of ascending aorta, prompt treatment of arrhythmias and low cardiac output, minimizing aortic cannulation or using off-pump bypass techniques, optimal regulation of metabolic state and cerebral perfusion, the prevalence of stroke in cardiac surgery patients with no evidence of significant carotid artery stenosis was found 1.8%[6,7].

The indication to treatment of patients with carotid disease should consider neurological symptomatology, degree of carotid stenosis, medical comorbidities, vascular and local anatomical features and carotid plaque morphology.

Neurological status is obviously an important predictor for stroke after CABG. It means that symptomatic patients are more vulnerable to compromised cerebral circulation during cardiopulmonary bypass. Patients were considered to be asymptomatic if they had no ipsilateral neurologic events of stroke, transient ischemic attack (TIA) or amaurosis fugax within the 6 months prior to the procedure. This definition used by ACST collaborative group which stated that neurologic symptoms older than 6 months should be considered asymptomatic because the risk of recurrent stroke decreases over time[8].

Carotid artery intervention to the neurological asymptomatic patients is one of the most controversial issues of vascular surgery throughout the last decades. Two randomized trials Asymptomatic Carotid Atherosclerosis Study (ACAS) and Asymptomatic Carotid Surgery Trial (ACST) are still remain cornerstone of guidelines and both study showed marked reduction in 5-year risk of stroke (50% relative risk reduction) in patients who had CEA[9,10]. Ten years result of ACST-1 trial reported that in comparison to conservative treatment CEA has retained a positive long-term effect on the reduction of all form of stroke. The absolute risk reduction 6.1% between surgical and conservative arm, carotid endarterectomy (CEA) showed a 46% reduction in the incidence of all strokes[11].

Because of the general lack of certainty about whether carotid revascularization is needed in individuals with asymptomatic disease, it's important to search answers of following questions before attempting to any intervention.

What is the Incidence of Significant Carotid Stenosis in Patients Undergoing CABG?

Current guidelines do not support routine screening for carotid artery stenosis before CABG because of given the low prevalence of stroke after CABG[4,6,12]. Most of the available evidence did not suggest casual relationship between a significant asymptomatic unilateral stenosis and post-CABG stroke[12]. Schoof et al. [5] reported that 94% of patients who suffered a stroke following cardiac surgery did not have a significant carotid stenosis.

One of the largest analysis of the prevalence of concomitant coronary and carotid atherosclerotic disease reported that the presence of internal carotid artery stenosis is directly related to the extent of CAD, though the prevalence of moderate and severe carotid stenosis in patients with CAD is lower than previously reported[13,14]. They had found severe carotid stenosis (>70%) in 7% among patients with three vessel CAD whereas this ratio decreases to 2% in patients with nonobstructive CAD. In patients below 70 years of age, prevalence of severe carotid disease decreases to 0.8% in male, 0.2% in women. Several studies have shown that the existence of bilateral moderate to severe carotid artery stenosis in ultrasound screened patients prior to cardiac surgery were found between 2.2 to 2.6% in patients undergoing CABG[15-17].

Does Untreated Asymptomatic Carotid Stenosis was Associated with an Increased Risk of Stroke After Cardiac Surgery?

The main question we faced is, what is the prevalence of perioperative stroke in neurologically asymptomatic patients with unilateral or bilateral carotid stenosis who undergoing to cardiac surgery without prophylactic CEA? Several studies included patients with both unilateral and bilateral 50-99% stenosis reported that 30-day risk of stroke was between 2% and 4.8% and perioperative death was between 2% and 6.5%[6,18-21]. Cardiac surgery patients with untreated asymptomatic 70-99% carotid stenosis incurred a 30-day stroke risk of only 2% and death/stroke rate of 4.8% was found in another meta-analysis[6,20]. However, due to relatively small numbers of these studies, it was not easy to reach statistically meaningful conclusion. The 30-day risk of death/stroke was 9.1% in asymptomatic patients with bilateral carotid disease following isolated cardiac surgery which shows higher risk than patients with unilateral disease[6,22]. Also, patients who described a history of stroke were significantly more likely (OR=3.6) to have further stroke than those who were asymptomatic[4]. Santarpino et al.[7] reported that among 649 patients with asymptomatic carotid artery stenosis >50% undergoing isolated CABG, the incidence of postoperative stroke was 1.5% and the risk of stroke were significant only in patients with a stenosis ³90% (OR=12, CI=1.4-33.3). They concluded as asymptomatic, severe carotid artery stenosis has a low prevalence and when left untreated is associated with a relatively low risk of postoperative stroke.

Does Concomitant CEA Procedure in Patients with Asymptomatic Carotid Disease Who Undergoing CABG Reduce Post-operative Incidence of Stroke?

Since the first report by Bernhard et al.[23] in 1972, in many centers, synchronous CEA and cardiac procedure has become routine practice. Because almost 80% of strokes are not preceded by TIA or minor strokes, preventing the risk of post-cardiopulmonary bypass strokes in asymptomatic patients by concomitant CEA is a sensible justification. But we need to clarify the procedural risk of the patients with bilateral carotid disease who have unilateral CEA then undergo cardiac surgery in the presence of an unoperated (contralateral) stenosis or occlusion.

Antoniou et al.[24] in their systematic review reported that patients undergoing CEA in the presence of an occluded contralateral carotid artery had increased incidence of stroke (OR=1,65, CI=1.3-2.1) and death (OR=1.76, CI=1.2-2.5) in 30-day of treatment compared with those with a patent contralateral carotid artery.

Studies reporting outcomes following staged/synchronous carotid revascularization prior to cardiac surgery have concluded that risk of procedural strokes are reduced[25,26]. Nwakanma et al.[27] reported that there was no significant difference in MI, stroke and death at 30-day follow-up between patients undergoing simultaneous CEA-CABG and isolated CABG. Baiou et al.[19] challenged the opinion that prophylactic CEA can be expected to significant reduce the risk of stroke in patients with asymptomatic carotid artery disease needs to cardiac surgery. However, they found that no strokes occurred in 61 consecutive open cardiac procedures in patients with asymptomatic severe unilateral carotid stenosis who did not undergo prophylactic CEA.

In the CABACS trial[28], patients with asymptomatic carotid stenosis, and with an indication for coronary surgical revascularization, were randomized to receive combined CEA with CABG versus CABG alone. Rates of stroke and death were in general higher than reported in some other studies, this could be possible due to relatively high risk and older population. Although not statistically different, the isolated CABG group tended to do better than did the combined procedure group (the 30-day and 1-year combined stroke/death rates were 18.5% and 23.4%, in the combined CEA/CABG group, and were 9.7% and 13.1% in the isolated CABG group).

What are the Surgical Options for CEA; Synchronous or Staged Approach? On-pump vs Off-pump?

Optimal surgical intervention and timing for patients having concomitant severe carotid and coronary artery stenosis remains uncertain. A hypothesis for the higher death and stroke rates is that combined procedures reveal higher operative stress, prolonged operative time and instability in hemodynamics on cardiac and cerebrovascular system[29]. There are different surgical techniques which can be chosen depending on patient status and characteristics of carotid disease. There seems to be no considerable difference in total vascular mortality and morbidity between two approaches. Synchronous CEA and CABG approach comparing with staged (prior) CEA requires only one anesthesia and has less risk of myocardial infarction while waiting for CABG. On the contrary, overall stroke risk seems to be lower with staged CEA than with synchronous CEA. In their meta-analysis of observational studies, Sharma et al.[30] reported that outcomes in combined and staged approach for synchronous CEA and CABG were similar therefore they suggest that the two strategies can be used interchangeable in the clinical practice depending on specific clinical conditions.

Feldman et al.[31] reported comparison of trends and in hospital outcomes of concurrent carotid artery revascularization and CABG in USA from the Nationwide Inpatient Sample (NIS) database between 2004 and 2012. During the 9-year period, they found 22,501 concurrent carotid revascularization and CABG during the same hospitalization, 68% of these patients underwent combined CEA plus CABG, 28% underwent staged CEA plus CABG and 3.6% underwent staged carotid stent (CAS) plus CABG. The adjusted risk of death was greater, whereas risk of stroke was lower with both combined CEA-CABG (stroke OR=0,65) and staged CEA-CABG (stroke OR=0.50) approaches compared with CAS-CABG[31].

Illuminati et al.[32] reported that in 185 patients with unilateral asymptomatic carotid stenosis >70%, randomized two groups, one group of patients received a CABG with previous or simultaneous CEA and another group of patients underwent CABG, followed by CEA. The 90-day stroke and death rate was 1.0% in synchronous group, 8.8% in delayed group (Odds ratio=0.11). They conclude that CEA before CABG or combined with CABG can prevent stroke better in patients with an asymptomatic severe carotid stenosis than delayed CEA[32].

Gopaldas et al.[33] identified from NIS database 1998 to 2007, 6153 patients who underwent CEA before or after CABG during the same hospital admission (staged) and 16639 patients who underwent both procedures on the same day (synchronous). They found that mortality (4.2% vs 4.5%) and neurologic complications (3.5% vs 3.9%) were similar between the staged and synchronous groups. Their subgroup analysis comparing on-pump and off-pump CABG which was performed within the staged and synchronous groups showed that performing off-pump CABG did not affect combined death-stroke rates in both groups. However, they reported that on-pump CABG was associated with an elevated risk of stroke in synchronous group (OR=1.55, CI=1.27-1.91) but not in staged patients[33].

In the literature, reported rate of mortality is between 0-4.5% and rate of stroke is between 0-3.1% for combined CEA and off-pump CABG[34-39]. Eren et al.[35] reported no stroke and 3.7% mortality for patients who had CEA and simultaneous off-pump CABG. Nabagiez et al.[36] suggested that twenty-four hour staged CEA followed by off-pump CABG minimizes post-CEA myocardial infarction while minimizing cerebrovascular accident post-CABG in patients with concomitant severe coronary and carotid artery disease. In order to comparison of early outcomes with three different approaches for combined CEA-CABG, Dönmez et al.[37] reported that no any further benefit with off-pump technique compared to on-pump technique, except for shorter intensive care unit and hospitalization times.

Shishehbor et al.[38] evaluated three approaches to carotid revascularization in CABG patients with asymptomatic carotid stenosis, staged CEA-CABG, combined CEA-CABG and staged carotid artery stenting (CAS)-CABG. They reported that combined CEA-CABG and staged CAS-CABG were associated with similar rates of stroke, death and MI in both groups but higher MI rates in the staged CEA-CABG group.

Khaitan et al.[39] reported simultaneous CEA and CABG during single cross-clamp, under 25°C of hypothermia for further cerebral protection, as a safe technique with a mortality rate of 5.8% and stroke incidence of 5.8%. Their assert was that systemic hypothermia reduces the metabolic tissue rate and is employed for neuroprotection during cardiac and aortic surgeries[39]. Guibaud et al.[40] also stated hypothermia below 28°C provides better cerebral protection especially for patients with bilateral carotid lesions. In contrast to this benefit, hypothermia during CEA had found to increase risk of MI (OR=3.5, CI=0.8-15.5) due to increased cross clamp and cardiopulmonary bypass times[37].

What are the Predictors Associated with Stroke After CABG?

Advanced age, prior cerebrovascular disease/stroke, severity of carotid artery stenosis and peripheral vascular disease, presence of contralateral carotid occlusion and porcelain ascending aorta, postoperative IABP or ECMO supporting, unstable angina, urgency of the procedure, prolonged cardiopulmonary bypass time and postoperative atrial fibrillations were reported as the most consistent independent predictors of perioperative stroke after CABG[7,41,42]. Gender, diabetes mellitus, hypertension, prior myocardial infarction, chronic renal failure and congestive heart failure showed contradictive results[7].

Post hoc analysis results of the NASCET and ACAS trials suggested that CEA may not be efficacious in women as it is in men[9,43]. Sarac et al.[44] reported that univariate results of 3077 consecutive patients who the ratio of men to women 2:1, results of gender differences revealed that women were higher risk for a postoperative stroke or mortality (3.1% for women, 2.1% for men; OR=1.6 CI=1.04-2.5) and also they found that female gender was an independent predictor (OR=1.7; CI=1.1-2.6) for a postoperative TIA or stroke.

How Can We Identify Vulnerable Carotid Plaque?

Risk stratification for carotid stenosis generally has been based on angiographic or Doppler ultrasonographic examination of luminal stenosis but we need to identify vulnerable carotid plaque by using more sophisticated methods such as positron emission tomography with computed tomography, magnetic resonance imaging (MRI), contrast enhanced ultrasound techniques and detection of micro-embolism using transcranial Doppler (TCD) ultrasound[45-50]. The pattern of progression of carotid stenosis is unpredictable and it may progress rapidly or slowly or remain stable in long term period[46]. Intimal wall thickening, increased echolucency, a low gray-scale median, lipid rich necrotic plaque core and plaque ulceration are the features of plaque itself which have been carried burden of risk of future stroke[47].

Detection of subclinical embolization or silent cerebral ischemic events may prove useful in identifying asymptomatic patients at high risk of stroke. The Asymptomatic Carotid Emboli Study was a multicenter prospective observational study aiming to investigate whether detection of asymptomatic embolic signals by use of TCD could predict stroke risk in patients with asymptomatic carotid stenosis[48]. The hazard ratio for the risk of ipsilateral stroke and TIA for those with embolic signals compared with those without was 7.57 (CI=2.32-24.6). They concluded that TCD can identify groups of patients with asymptomatic carotid stenosis who are at low or high risk of future stroke[48].

Kakkos et al.[49] tested the hypothesis that the size of a juxtaluminal black (hypoechoic) area (JBA) in ultrasound images of asymptomatic carotid artery plaques predicts future ipsilateral ischemic stroke. They conclude that the concept of plaque heterogeneity and plaque with a large JBA can be used for stroke risk stratification.

Measuring carotid plaque volume (CPV) by minimally invasive tomographic ultrasound imaging and MRI suggested that CPV was associated with cardiovascular risk factors and symptoms of cerebral ischemia[50,51]. Ball et al.[50] reported that CPV correlated with symptoms of cerebral ischemia but not carotid stenosis and it could be a potential indicator for CEA. To investigate the association between MR imaging-depicted intraplaque hemorrhage (IPH) in the carotid artery wall and the risk of future ipsilateral cerebrovascular events in men with asymptomatic moderate carotid stenosis, Singh et al.[52] reported that MR-depicted IPH was associated with an increased risk of cerebrovascular events (HR=3.59 CI=2.4-4.7, negative predictive value=100%).

Guidelines Recommendations for the Treatment of Asymptomatic Carotid Stenosis in Coronary Artery Bypass Patients

Clinical Practice Guidelines of the European Society for Vascular Surgery in 2017[12] recommend that a staged or synchronous carotid intervention is not recommended in coronary artery bypass patients with an asymptomatic unilateral 70-99% carotid stenosis for the prevention of stroke after coronary bypass (Class III, level C). A staged or synchronous carotid intervention may be considered in coronary artery bypass patients with bilateral asymptomatic 70-99% carotid stenosis or a 70-99% stenosis with contralateral occlusion (Class IIB, level C). The choice between carotid endarterectomy and carotid stenting in whom a carotid intervention is deemed necessary prior to CABG should be based on the urgency of performing surgery, choice of antiplatelet strategy during CABG, individual patient characteristics, symptoms and local expertise (Class IIa, level C).

Conclusion

The decision about how to manage asymptomatic carotid disease in the setting of planned CABG becomes more complex due to surgical treatment of either pathology may be complicated by multiple factors. In routine clinical practice, the indication to CEA is usually based on symptoms and severity of stenosis. Meticulous screening for carotid disease to identifying high risk patients who have vulnerable plaque is one of the most crucial part of this conundrum. Synchronous or staged CEA still remain valuable options in order to diminish postoperative risk of stroke for neurologically asymptomatic patients who have bilateral significant carotid artery stenosis or contralateral occlusion undergoing to CABG. But these group of patients are relatively small proportion of asymptomatic patients who needs to CABG. Because of the low rate of stroke in uncomplicated patients who have combined CEA and CABG, synchronous CEA-CABG procedure can be recommended in asymptomatic men below 75 years old with a critical unilateral suspected carotid plaque >80% stenosis if the expected perioperative stroke/death rate is <3%. The majority of patients undergoing CABG have asymptomatic unilateral carotid stenosis and it seems rationale to leaving the low risk patients to be treated medically when considering insignificant stroke rate of these untreated carotid disease.

Ethics

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References

1. Nichols M, Townsend N, Luengo-Fernandez R, et al. European cardiovascular disease statistics 2012. European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis.

2. Eascott HH, Pickering GW, Rob CG. Reconstruction of internal carotid artery in a patient with intermittent attacks of hemiplegia. Lancet 1954;267:994-6.
3. Kapetanakis EI, Stamou SC, Dullum MK, et al. The impact of aortic manipulation on neurologic outcomes after coronary artery bypass surgery: a risk adjusted study. Ann Thorac Surg 2004;78:1564-71.
4. Naylor AR, Mehta Z, Rothwell PM, Bell PRF. Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature. Eur J Vasc Endovasc Surg 2002;23:283-94.
5. Schoof J, Lubahn W, Baerner M, et al. Impaired cerebral autoregulation distal to carotid stenosis/occlusion is associated with an increased risk of stroke with cardiopulmonary bypass. J Thorac Cardiovasc Surg 2007;134:690-6.
6. Naylor AR, Bown MJ. Stroke after cardiac surgery and its association with asymptomatic carotid disease: an updated systematic review and meta-analysis. Eur J Vasc Endovasc Surg 2011;41:607-24.
7. Santarpino G, Nicolini F, De Feo M, et al. Prognostic impact of asymptomatic carotid artery stenosis in patients undergoing coronary artery bypass grafting. Eur J Vasc Endovasc Surg 2018;56:741-8.
8. Nedeltchev K, Pattynama PM, Biaminoo G et al. Standardized definitions and clinical endpoints in carotid artery and supra-aortic trunk revascularization trials. Catheter Cardiovasc Interv 2010;76:333-44.
9. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for Asymptomatic Carotid Atherosclerosis Study. JAMA 1995;273:1421-8.
10. Halliday A, Mansfield A, Marro J. The MRC Asymptomatic Carotid Surgery Trial (ACST): carotid endarterectomy prevents disabling and fatal carotid territory strokes. Lancet 2004;363:1491-502.
11. Halliday AH, Harrison M, Hayter E, et al. 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicenter randomized trial. Lancet 2010;376:1074-84.
12. Naylor AR, Ricco JB, de Borst GJ, et al. Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2018;55:3-81.
13. Steinvil A, Sadeh B, Arbel Y, et al. Prevalence and predictors of concomitant carotid and coronary artery atherosclerotic disease. J Am Coll Cardiol 2011;57:779-83.
14. Kallikazaros I, Tsioufis C, Sideris S, et al. Carotid artery disease as a marker for presence of severe coronary artery disease in patients evaluated for chest pain. Stroke 1999;30:1002-7.
15. Wanamaker KM, Moraca RJ, Nitzberg D, et al. Contemporary incidence and risk factors for carotid artery disease in patients referred for coronary artery bypass surgery. J Cardiothorac Surg 2012;7:78.
16. Stamou SC, Hill PC, Dangas G, et al. Stroke after coronary artery bypass: incidence, predictors and clinical outcome. Stroke 2001;32:1508-13.
17. Naylor AR. Why is the management of asymptomatic carotid disease so controversial? The Surgeon 2015;13:34-43.
18. Li Y, Walicki D, Mathiesen C, et al. Strokes after cardiac surgery and relationship to carotid stenosis. Arch Neurol 2009;66:1091-6.
19. Baiou D, Karageorge A, Spyt T, et al. Patients undergoing cardiac surgery with asymptomatic unilateral carotid stenoses have a low risk of peri-operative stroke. Eur J Vasc Endovasc Surg 2009;38:556-9.
20. Ghosh J, Murray D, Khwaja N, et al. The influence of asymptomatic significant carotid disease on mortality and morbidity in patients undergoing coronary artery bypass surgery. Eur J Vasc Endovasc Surg 2005;29:88-90.
21. Safa TK, Friedman S, Mehta M, et al. Management of coexisting coronary artery and asymptomatic carotid artery disease: report of a series of patients treated with coronary bypass alone. Eur J Vasc Endovasc Surg 1999:17:249-52.
22. Manabe S, Shimokawa T, Fukui T, et al. Influence of carotid artery stenosis on stroke in patients undergoing off-pump coronary artery bypass grafting. Eur J Cardiothorac Surg 2008;34:1005-8.
23. Bernhard VM, Johnson WD, Peterson JJ. Carotid artery stenosis. Association with surgery for coronary artery disease. Arch Surg 1972;105:837-40.
24. Antoniou GA, Kuhan G, Sfyroeras GS, et al. Contralateral occlusion of the internal carotid artery increases the risk of patients undergoing carotid endarterectomy. J Vasc Surg 2013;57:1134-45.
25. Timaran CH, Rosero EB, Smith ST, et al. Trends and outcomes of concurrent carotid revascularization and coronary bypass. J Vasc Surg 2008;48:355-60.
26. Naylor AR. Synchronous cardiac and carotid revascularization: the devil is in the detail. Eur J Vasc Endovasc Surg 2010;40:303-8.
27. Nwakanma L, Poonyagariyagom HK, Bello R, et al. Early and late results of combined carotid endarterectomy and coronary artery bypass versus isolated coronary artery bypass. Interact Cardiovasc Thorac Surg 2006;5:159-65.
28. Weimar C, Bilbilis K, Rekowski J, et al. Safety of simultaneous coronary artery bypass grafting and carotid endarterectomy versus isolated coronary artery bypass grafting (CABACS). A randomized clinical trial. Stroke 2017;48:2769-75.
29. Ogutu P, Werner R, Oertel F, et al. Should patients with asymptomatic significant carotid stenosis undergo simultaneous carotid and cardiac surgery? Interact Cardiovasc Thorac Surg 2014;18:511-8.
30. Sharma V, Deo SV, Park SJ, et al. Meta-analysis of staged versus combined carotid endarterectomy and coronary artery bypass grafting. Ann Thorac Surg 2014;97:102-9.
31. Feldman DN, Swaminathan RV, Geleris JD, et al. Comparison of trends and in-hospital outcomes of concurrent carotid artery revascularization and coronary artery bypass graft surgery. J Am Coll Cardiol 2017;10:286-98.
32. Illuminati G, Ricco JB, Caliò F, et al. Short-term results of a randomized trial examining timing of carotid endarterectomy in patients with severe asymptomatic unilateral carotid stenosis undergoing coronary artery bypass grafting. J Vasc Surg 2011;54:998-9.
33. Gopaldas RR, Chu D, Dao TK, et al. Staged versus synchronous carotid endarterectomy and coronary artery bypass grafting: Analysis of 10-year nationwide outcomes. Ann Thorac Surg 2011;91:1323-9.
34. Fareed KR, Rothwell PM, Mehta Z, et al. Synchronous carotid endarterectomy and off-pump coronary bypass: an updated, systematic review of early outcomes. Eur J Vasc Endovasc Surg 2009;37;375-8.
35. Eren E, Balkanay M, Toker ME, et al. Simultaneous carotid endarterectomy and coronary revascularization is safe using either on-pump or off-pump technique. Int Heart J 2005;46:783-93.

36. Nabagiez JP, Bowman KC, Shariff MA, et al. Twenty-four hour staged carotid endarterectomy followed by off-pump coronary bypass grafting for patients with concomitant carotid and coronary disease. Ann Thorac Surg 2014;98:1613-8.

37. Dönmez A, Adademir T, Sacli H, et al. Comparison of early outcomes with three approaches for combined coronary revascularization and carotid endarterectomy. Braz J Cardiovasc Surg 2016;31:365-70.

38. Shishehbor MH, Venkatachalam S, Sun Z, et al. A direct comparison of early and late outcomes with three approaches to carotid revascularization and open heart surgery. J Am Coll Cardiol 2013;62:948-56.

39. Khaitan L, Sutter FP, Goldman SM, et al. Simultaneous carotid endarterectomy and coronary revascularization. Ann Thorac Surg 2000;69:421-4.

40. Guibaud JP, Roques X, Laborde N, et al. Extracorporeal circulation as an additional method for cerebral protection in simultaneous carotid endarterectomy and coronary artery surgical revascularization. J Card Surg 2004;19:415-9.

41. Mao Z, Zhong X, Yin J, et al. Predictors associated with stroke after coronary artery bypass grafting: a systematic review. J Neurol Sci 2015;357:1-7.

42. Faggioli G, Pini R, Mauro R, et al. Contralateral carotid occlusion in endovascular and surgical carotid revascularization: a single center experience with literature review and meta-analysis. Eur J Vasc Endovasc Surg 2013; 46:10-20.

43. Inzitari D, Eliasziw M, Gates P, et al. The North American Symptomatic Carotid Endarterectomy Trial Collaborators. The causes and risk of stroke in patients with asymptomatic internal carotid artery stenosis. N Engl J Med 2000;342:1693-700.

44. Sarac TP, Hertzer NR, Mascha EJ, et al. Gender as a primary predictor of outcome after carotid endarterectomy. J Vasc Surg 2002;35:748-53.

45. Jayasooriya G, Thapar A, Shalhoub J, et al. Silent cerebral events in asymptomatic carotid stenosis. J Vasc Surg 2011;54:227-36.

46. Conrad MF, Baloum V, Mukhopadhyay S, et al. Progression of asymptomatic carotid stenosis despite optimal medical therapy. J Vasc Surg 2013;58:128-35.

47. Kakkos SK, Nicolaides AN, Charalambous I, et al. Predictors and clinical significance of progression or regression of asymptomatic carotid stenosis. J Vasc Surg 2014;59:956-67.

48. Markus H, King A, Shipley M, et al. Asymptomatic embolization for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study. Lancet Neurol 2010;9:663-71.

49. Kakkos SK, Griffin MB, Nicolaides AN, et al. The size of juxtaluminal hypoechoic area in ultrasound images of asymptomatic carotid plaques predicts the occurence of stroke. J Vasc Surg 2013;57:609-18.

50. Ball S, Rogers S, Kanesalingam K, et al. Carotid plaque volüme in patients undergoing carotid endarterectomy. Br J Surg 2018;105:262-9.

51. Zhao H, Zhao X, Liu X, et al. Association of carotid atherosclerotic plaque features with acute ischemic stroke: a magnetic resonance imaging study. Eur J Radiol 2013;82:e465-70.

52. Singh N, Moody AR, Gladstone DJ, et al. Moderate carotid artery stenosis: MR imaging-depicted intraplaque hemorrhage predicts risk of cerebrovascular ischemic events in asymptomatic men. Radiology 2009;252:502-8.

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Prevalence and Predictors of Cognitive Impairment Among Hypertensive Patients on Follow Up at Jimma University Medical Center, Jimma, Southwest Ethiopia

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Abstract

Objectives: Cognitive impairment is when a person has suffered recalling, learning new things, concentrating, or making decisions that affect his/her everyday life. Hypertension induces vascular alteration and lead to cognitive impairment by leading to hypoperfusion, ischemic and hemorrhagic stroke, and white matter injury.

This study aimed to determine the prevalence and predictors of cognitive impairment among hypertensive patients on follow up at Jimma University Medical centre, Jimma, Southwest Ethiopia.

Materials and Methods: Institution based cross sectional study design was employed from June 01 to July 15, 2018 among 279 hypertensive patients on follow-up at Jimma University Medical Centre chronic clinic, Jimma, Ethiopia. The collected data were cleared and entered into SPSS Version 20.0 for analysis. The association between the independent variables and the outcome variable (cognition level) was analyzed using logistic regression model. A p value of <0.05 was considered statistically significant in the final model.

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Abstract

Results: Out of the 279 hypertensive patients included in this study, 142 (50.9%) were male and the remaining proportion was female. The mean age ± SD of the participants was 53.15 + 11.544 years with a range of 20 to 86 years. The prevalence of cognitive impairment in this study was 86 (30.8%). Triglycerides level > 200 mg/dL (AOR=3.570, 95% CI=1.598-2.977) and high blood pressure Stage II HTN were significantly associated with cognitive impairment (AOR=2.649, 95% CI=4.191-5.391).

Conclusion: Cognitive impairment was relatively common in the study population. The study revealed that, high triglyceride levels and Stage II HTN were significantly associated with cognitive impairment.

Keywords: Cognition, cognitive impairment, hypertension, MMSE, Jimma University

Introduction

Cognition states the processing of information, applying knowledge and changing preference. Cognitive function majorly includes focused attention, executive function, recall, producing and understanding language, solving problem, and making decisions[1].

Hypertension, a chronic elevation in blood pressure exceeding 140 mmHg systolic (SBP) or 90 mmHg diastolic (DBP), can lead to target organs to be damaged (brain, heart and kidneys) by inducing detrimental events. Cerebral blood vessels are the main target of the deleterious effects of hypertension on the brain[2]. Hypertension causes typical alterations in small arteries and arterioles supplying the subcortical and basal ganglia white matter, resulting in small vessel disease, a major cause of lacunar strokes and cerebral hemispheric white matter damage. The resulting structural and functional cerebrovascular alterations underlie many of the neuron pathological abnormalities responsible for the cognitive deficits, including white matter damage, micro infarcts, micro bleeds, silent brain infarcts, and brain atrophy[3]. Hypertension induces vascular alteration and leads to cognitive impairment by causing hypoperfusion, ischemic and hemorrhagic stroke, and white matter injury[4]. Hypertension is also a risk factor for lowered cognitive function in persons without clinically diagnosed stroke and dementia[5]. Moreover, reduced abstract reasoning (executive dysfunction), slowing of mental processing speed and memory deficits are reported in association with hypertension[4]. Hypertensive elderly individuals appear to demonstrate declines in measures of global cognition[6], including working memory[7], attention[8], and executive functioning[9]. A study conducted about the effects of hypertension on cognitive function with emphasis on psychomotor speed of air traffic controllers and pilots since the 1960s demonstrated reduced performance in individuals with hypertension[10].

Cognitive deficits due to HTN in adults can be difficult to detect but can be divided into several domains including learning, memory, and attention[11]. The blood vessels in the prefrontal subcortical areas are often affected by severe HTN, which can affect the ability to make executive decisions (e.g., planning, attention, problem solving, verbal reasoning, etc.)[12].

Hypertension is one of recent growing public health problem in many developing countries including Ethiopia. In Ethiopia, there is no study published on cognitive impairment among hypertensive patients. Therefore, the results of this study will help health policy makers to give special considerations for cognitive impairment among hypertensive patients during designing diagnosis and management strategies. The study results will be used particularly in counseling of the prevention of the risk factors. It identifies modifiable risk factors. It also adds additional knowledge besides the existing literature. This study is important for further researchers as a baseline for study on this area.

Materials and Methods

Study Area and Period

The study was conducted at Jimma University Medical Center (JUMC), Chronic illnesses Clinic in Jimma town. Jimma town is located 352 km Southwest of Addis Ababa, the capital city of Ethiopia. JUMC is one of the oldest university hospitals in Ethiopia. Currently, it is one of the teaching and referral hospitals in the Southwestern part of the country, providing services for approximately 15 million people in the catchment area, including chronic follow up for diabetes mellitus, hypertension and other chronic cases (hospital record). The study was conducted from June 01 to July 15, 2018.

The source population of this study was all adults. Hypertensive patients on follow up at JUMC chronic illnesses clinic were our target population. The study subjects were those hypertensive patients attending chronic illnesses clinic, fulfilling eligibility criteria and willing to participate. All hypertensive patients and those who had complete medical records were included. Those with a known cognitive impairment (psychiatric disorder, severe medical illnesses, and previous history of stroke) and those with visual, hearing, and speech difficulty were excluded from the current study.

Sample Size and Sampling Technique

The actual sample size was determined by using the single population proportion formula, where the following assumptions were considered: 50% prevalence, 95% confidence interval, and 5% margin of error. Since the total population included 740 patients, we employed a correction formula, and then 10% nonresponse rate was added, which gave rise to a final sample size of 279. The participants were selected through the systematic random sampling technique after having the monthly client flow to the hospital.

Data Collection Technique

Data were collected by using an interviewer-administered structured questionnaire prepared particularly for this study, adapted from WHO STEP wise approach for chronic disease risk factor surveillance[13]. The questionnaire was prepared in English language, translated to local languages and then translated back to English to check for consistency. The questionnaire was developed based on the study objectives. The questionnaire contained socio-demographic factors, clinical variables such as blood pressure, behavioral variables and anthropometric measurements of body weight, height and waist circumference.

To measure cognitive function, the standard validated MMSE tool containing five components [orientation (10 points), registration (3 points), calculation (5 points), recall (3 points), language and drawing (9 points)] was used. The total score obtained for each study subject was 30.

Chart review checklist was used to collect data concerning clinical variables (recorded laboratory results). Blood pressure was measured by using the Omron digital blood pressure measuring device. For each patient, three measurements were performed at two-minute intervals and then the average was taken as the final data for analysis[13].

Waist circumference was measured with a flexible inelastic tape placed on the midpoint between the lower rib margin and the iliac crest in a perpendicular plane to the long axis of the body. Height and weight were measured by using a portable Stadiometer. Body mass index (BMI) was calculated by using a person's body weight in kg and body height in meters. The formula used was BMI = kg/m^2 where kg is a person's weight in kilograms and m^2 is their height in meters squared. Four data collectors (two BSc nurses and two psychiatry nurses) were involved in data collection and collection process was supervised.

Operational Definitions

- **Cognitive impairment**: Is when a person has trouble remembering, recall, orientation, registration, attention and calculation, language and praxis.
- **Mini Mental State Examination (MMSE):** Is a commonly used 30-point scale for assessing cognitive

function in orientation, registration, attention and calculation, recall, language, and drawing. MMSE administration was performed according to existing standards[14].

Hypertension: A person having SBP of 140 mmHg and/or DBP of 90 mmHg and above.

- **Controlled BP** = SBP 120-139 and DBP 80-89
- **Stage I HTN** = SBP 140-159 and DBP 90-99
- **Stage II HTN** = SBP $\geq$160 and DBP $\geq$100

Physical activity: According to WHO, adults and older adults are recommended to do a minimum of 150 moderate -intensity or 75 min vigorous intensity aerobic activity or their equivalent combination per week, and muscle strengthening activity or at least 30 minutes of moderate intensity activity on 5 days a week.

Statistical Analysis

Data were cleaned and entered into the computer using Epi-Data version 3.1 and exported to the Statistical Package for Social Science (SPSS) version 20.0 for analysis. Frequency, percentage and mean were computed for descriptive statistics. The association between the independent and dependent variables were analyzed using the logistic regression model. Bivariate analysis was done to select candidates for multivariate at $p<0.25$. From the multivariate logistic regression, independent variables having a p value of <0.05 with 95% confidence interval were declared as significantly associated with cognitive impairment. Finally, model fitness was checked through the Hosmer and Lameshow test ($p>0.05$). Results were organized by using frequency tables, graphs, and charts.

Data quality assurance

The following measures were taken to assure quality of data: before data collection, data collectors were trained on the objectives of the study, interviewing, on chart review contents and measurement techniques by the principal investigator for one day. The data collection instruments were pre-tested on the hypertensive patients at Shene Gebe Hospital (on 5% of the sample size) and necessary modifications were made based on the results of the pre-test. Data were checked for completeness within 24 hours. Data cleaning and verification were done before entering them into SPSS.

Ethical consideration

The study was conducted after receiving ethical approval from Jimma University Ethical Review Board. Permission letter was obtained from Jimma University Institute of Health Ethical Review Board (No: IRB/098/2018) before data collection was started. Written informed consent was obtained from all study participants. Data obtained during the study were treated confidentially. The right to withdraw from the study was respected for participants.

Results

Socio-demographic Characteristics of Study Participants

A total of 294 hypertensive patients were enrolled into the study. Due to incomplete information on the laboratory records, 15 patients were not included in the analysis and hence the final analysis included 279 subjects. Out of 279 hypertensive patients included, 142 (50.9%) were males. The mean age of participants was 53.15$\pm$11.544 years with range of 20 to 86 years. Around two- third of them [178 (63.8%)] were in age group between 40 and 59 years. Educational status of more than half of participants 153 (54.8) was grade 8 and lower (As indicated in Table 1).

Behavioral Factors and Clinical Factors

About 94 (33.7%) respondents were Khat chewers. Regarding the status of smoking, 18 (6.5%) were cigarette smokers. Forty-nine (17.6%) respondents were alcohol drinkers. Most of them [237 (84.9%)] were physically active. Around one-fourth of the respondents, 67 (24.0%) had high triglycerides levels, 33 (11.8%) had high cholesterol levels and 28 (10.0%) had high low-density lipoprotein levels. Abnormal high-density lipoprotein levels in males and females were 50 (17.9%) and 74 (26.5%), respectively. The duration of diagnosis was <5 years in almost half of the respondents [137 (49.1%)]. Above half of the respondents [148 (53%)] were on medication for a duration of <5 years. Around one-fourth [69 (24.7%)] of respondents' blood pressure values were high (both SBP and DBP). Half [140 (50.2%)] of the participants body weights were abnormal, above twenty-five (Table 2).

Predictors of cognitive impairment

Table 3 shows the result of the bivariate and multivariate logistic regression analyses. In the bivariate analysis, socio-demographic factors such as age group between 40 and 59 years and above 60 years were significantly associated with cognitive impairment (COR=0.524; 95% CI=0.199-1.384 and COR=2.694; 95% CI=0.990-7.530, respectively). Additionally, being men (COR=0.552, 95% CI=0.329-0.924) and educational status of grade 8 and lower and grade 9-12 group (COR=2.671; 95% CI=1.364-5.230 and COR=0.571; 95% CI=0.211-1.477) were significantly associated with cognitive impairment.

Among behavioral factors, Khat chewing, cigarette smoking and alcohol were significantly associated with cognitive impairment (COR=1.449, 95% CI=0.854-2.460, COR=1.466, 95% CI=0.548-3.921, COR=0.447, 95% CI=0.206-0.969, respectively). Furthermore, physical inactivity was significantly associated with cognitive impairment (COR=2.355, 95% CI=1.207-4.598).

The analysis of clinical state- related factors, cholesterol level above 240 mg/dL and triglycerides above 200 mg/dL (COR=2.997, 95% CI=1.593-5.570) were also detected to be associated with cognitive impairment. Moreover,

Table 1. Socio-demographic characteristics of hypertensive patients studied for cognitive impairment at follow up in chronic illnesses clinic, JUMC, 2018

Variable (n=279)	Frequency, n (%) Sex
Sex	
Male	142 (50.9)
Female	137 (49.1)
Age	
20-39	22 (7.9)
40-59	178 (63.8)
60+	79 (28.3)
Educational status	
Grade 8 and lower	153 (54.8)
Grade 9-12	60 (21.5)
College and above	66 (23.7)
Family history of HTN	
Yes	77 (27.6)
No	202 (72.4)
Khat chewing	
Yes	94 (33.7)
No	185 (66.3)

HTN: Hypertension

Table 2. Clinical state-related factors and physical measurement characteristics of hypertensive patients studied for cognitive impairment at follow up in chronic illnesses clinic, JUMC, 2018

Variables (n=279)	Frequency (%)
Khat chewing	
Yes	94 (33.7)
No	185 (66.3)
Cigarettes smoking	
Yes	18 (6.5)
No	261 (93.5)
Alcohol	
Yes	49 (17.6)
No	230 (82.4)
Physical activity	
Inactive	42 (15.1)
Active	237 (84.9)
Total cholesterol (mg/dL)	
<200	192 (68.8)
201-239	54 (19.4)
>240	33 (11.8)
Triglyceride (mg/dL)	
<150	132 (47.3)
151-199	80 (28.7)
≥200	67 (24.0)

BMI of 18.5-24.9 and >25 (kg/m²) was associated with cognitive impairment (COR=3.181, 95% CI=1.079-9.384, COR=1.375, 95% CI=0.089-2.337). Finally, HTN stage II was found to be related to cognitive impairment (COR=2.363, 95% CI=1.252-4.459).

Hosmer lame show (p=0.732), the model was fit for Hosmer-Lemeshow. Multivariable logistic regression analysis was done for all explanatory variables having p<0.25 in the bivariate logistic regression analysis. However, on the multivariable analysis, the variables of triglycerides ≥200 mg/dL and HTN stage II were found to be significantly associated with cognitive impairment.

Therefore, those who had triglycerides ≥200 mg/dL were 3.5 times more likely to have cognitive impairment than those who had triglycerides below 150 mg/dl. (AOR=3.570, 95% CI=1.598-2.977). Finally, those who had high blood pressure of Stage II HTN were 2.6 times more likely to have cognitive impairment than those who had controlled HTN (AOR=2.649, 95% CI=4.191-5.391) (Table 3).

Discussion

In this study, the prevalence of cognitive impairment in those who scored less than 24 out of 30 points by using MMSE was found to be 30.8%. This is higher than the results obtained in Brazil and China, which were 23% and 15.4%, respectively[15,16]. This discrepancy might be due to poor blood pressure control, educational level and institutional based study. On the other hand, this study is less than the study conducted in Peru and Iran, 63.3% and 61.5%, respectively[17,18]. These differences might be due to the differences in sample size, which was lower in our study, and due to the fact that these two studies included comorbid diseases in contrast to ours.

In our study, participants with triglycerides above 200 mg/dL were independent predictors of cognitive impairment, which was agreed by thestudies done in Egypt and China[19,20]. The possible mechanism may be due to that hypertriglyceridemia changes cerebral blood vessels by increasing the viscosity of blood and lowers cognitive function by causing arteriosclerosis[21]. Similarly, a study conducted in China suggests that higher normal concentrations of TG were significantly negatively associated with cognitive impairment[22].

In this study, participants with high blood pressure were independent predictors of cognitive impairment, which was in line with the studies done in India, UK, Pittsburgh, Angola and Birmingham, respectively[23-25]. High blood pressure alters cerebrovascular structure and function, which leads to brain lesions such as cerebral atrophy, stroke and lacunar infarcts, diffuse white matter damage, micro infarcts and micro bleeds, and finally results in cognitive impairment. Possible molecular mechanism of this pathology may be because high blood pressure impairs the metabolism and transfer of amyloid-β protein (Aβ), accelerating cognitive impairment[26]. Damage to vascular endothelial cell function leads to a reduction in the ability of endothelial cells to regulate microvascular flow and to exert their antithrombotic and antiatherogenic effects[27], which results in the reduction of resting cerebral blood flow, which intern causes decrease in oxygen and nutrient result in impaired Aβ trafficking and promoting amyloid aggregation, finally pre-neural inflammation and death lead to cognitive loss[28].

Limitations of the Study

The cross-sectional study design does not provide evidence of a cause and effect relationship.

Lack of imaging data confines the ability to link hypertension and its causingneuropathology.

Undiagnosed mental illnesses and severe comorbid diseases might have affected the performance of the study subjects on the MMSE items, and then on the overall score.

Conclusion

Cognitive impairment was relatively common in our study population. The study revealed that triglycerides above 200 mg/dL and HTN stage II were the predictors of cognitive impairment.

Table 3. Predictors of cognitive impairment among hypertensive patients at follow up clinic of JUMC, 2018

	Variable Cognitive impairment				Bivariate Analysis Multivariate Analysis	
	Yes	**No**	**p**	**COR (95% CI)**	**p**	**AOR (95% CI)**
Age						
20-39	7	15	1	1	1	1
40-59	35	143	0.192	0.524 (0.199-1.384)	0.115	0.412 (0.136-1.242)
60+	44	35	0.052	2.694 (0.990-7.330)	0.199	2.088 (0.678-6.430)
Sex						
Male	35	107	0.024	0.552 (0.329-0.924)	0.069	0.534 (0.272-1.049)
Female	51	86	1	1	1	1
Educational status						
Grade 8 and lower	64	89	0.004	2.671 (1.364-5.230)	0.386	1.447 (0.627-3.337)
Grade 9-12	8	52	0.248	0.571 (0.221-1.477)	0.067	0.325 (0.107-0.984)
College and above	14	52	1	1	1	1
Familial history						
Yes	25	52	0.714	1.111 (0.632-1.953)		
No	61	141	1	1		
Khat chewing						
Yes	34	60	0.169	1.449 (0.854-2.460)	0.821	1.083 (0.543-2.161)
No	25	133	1	1	1	1
Cigarette smoking						
Yes	7	11	0.446	1.466 (0.548-3.921)		
No	79	182	1	1		
Alcohol						
Yes	9	40	0.041	0.447 (0.206-0.969)	0.086	086 0.449 (0.180-1.121)
No	77	153	1	1	1	1
Physical activity						
Inactive	20	22	0.012	2.355 (1.207-4.598)	0.129	2.088 (0.678-6.430)
Active	66	171	1	1	1	1
Cholesterol						
<200	53	139	1	1	1	1
201-239	18	36	0.413	1.311 (0.686-2.508)	0.778	1.121 (0.507-2.481)
≥240	15	18	0.040	2.186 (1.024-4.649)	0.333	1.626 (0.608-4.380)
TG						
<150	31	101	1		1	1
151-199	23	57	0.394	1.315 (0.700-2.467)	0.307	1.518 (0.682-3.379)
>200	32	35	0.001	2.979 (1.593-5.570)	0.002	3.570 (1.598-2.977)

Table 3. Continued

	Variable Cognitive impairment			Bivariate Analysis Multivariate Analysis		
	Yes	No	p	COR (95% CI)	p	AOR (95% CI)
BMI (kg/m³)						
<18.5	8	7	1	1	1	
18.5-24.9	41	83	0.036	3.181 (1.079-9.384)	0.428	0.610 (0.180-2.071)
>25	37	103	0.239	1.375 (0.089-2.337)	0.272	0.469 (0.138-1.748)
BP (SBP/DBP)						
<140 and 90	29	84	1	1	1	1
Stage I HTN	26	71	0.851	1.061 (0.573-1.965)	0.218	1.588 (0.751-3.317)
Stage II HTN	31	38	0.008	2.363 (1.252-4.459)	0.017	2.649 (4.191-5.391)

HTN: Hypertension, BMI: Body mass index, TG: Triglyceride, CI: Confidence interval, AOR: Adjusted Odds ratio, COR: Combined ratio

Based on our findings, the following recommendations were forwarded:

Recommendation

The JUMC should plan periodic screening of cognitive impairment among hypertensive patients to prevent further complications.

The JUMC health professionals should promote screening triglyceride and ever visit to reduce risk of cognitive impairment.

The JUMC health professionals should increase the frequency of the monitoring of patients' blood pressures in order to reduce the risk of cognitive impairment.

Moreover, the Federal Ministry of Health should promote the implementation of strategies for screening of cognitive impairment before the development of complications.

Finally, further researchers should measure clinical factors rather than chart review and they should use imaging modalities to explore the extent of cognitive impairment on hypertensive patients.

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Ethics

Ethics Committee Approval: The study was conducted after receiving Ethical approval from Jimma University Ethical Review Board. Permission Letter was obtained from the Institute of Health Sciences Ethical review board, Jimma University (No: IRB/098/2018) before data collection was started.

Informed Consent: Informed consent was taken from each study participant before data collection.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.E.B., Concept: T.E.B., B.G., D.D., Design: T.E.B., M.A.K., Data Collection or Processing: T.E.B., A.G., M.A.K., Analysis or Interpretation: T.E.B., A.G., Literature Search: T.E.B., Writing: T.E.B., B.G., D.D.

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References

1. Jeganathan J, Seemanthini TS. Memory Impairment in Young Type 2 Diabetes Mellitus Males: An Alarming Concern! Glob J Res Anal 2014;3:172-3.
2. Perrotta, M, Lembo G, Carnevale, D. Hypertension and dementia: epidemiological and experimental evidence revealing a detrimental relationship. Int J Mol Sci 2016;17:347.
3. Shi Y, Wardlaw JM. Update on cerebral small vessel disease: a dynamic whole-brain disease. Stroke Vasc Neurol 2016;25:83-92.
4. Iadecola C, Yaffe K, Biller J, et al. Impact of hypertension on cognitive function: a scientific statement from the American Heart Association. Hypertension 2016;68:e67-94.
5. Waldstein SR. The relation of hypertension to cognitive function.Curr. Dir. Psychol Sci 2003;12:9-12.
6. Goldstein FC, Levey AI, Steenland NK. High blood pressure and cognitive decline in mild cognitive impairment. J Am Geriatr Soc 2013;61:67-73.
7. Elias MF, Dore GA, Davey A, et al. From blood pressure to physical disability: the role of cognition. Hypertension 2010;55:1360-5.
8. Hannesdottir K, Nitkunan A, Charlton RA, et al. Cognitive impairment and white matter damage in hypertension: a pilot study. ActaNeurol Scand 2009;119:261-8.
9. Waldstein SR, Brown JR, Maier KJ, et al. Diagnosis of hypertension and high blood pressure levels negatively affect cognitive function in older adults. Ann Behav Med 2005;29:174-80.
10. Elias MF, Goodell AL, Dore GA. Hypertension and cognitive functioning: a perspective in historical context. Hypertension 2012;60:260-8.
11. Si C, Ren C, Wang P, et al. Impairment in preattentive processing among patients with hypertension revealed by visual mismatch negativity. BioMed Res Int 2014;2014:945121.
12. Cha SD, Patel HP, Hains DS, et al. The effects of hypertension on cognitive function in children and adolescents. Int J Pediatr 2012;2012:891094.
13. Organization WHO. Universal health coverage on the journey towards Healthy Islands in the Pacific. Manila: WHO Regional Office for the Western Pacific. https://apps.who.int/iris/handle/10665/275483
14. Mitchell AJ, Shukla D, Ajumal HA, et al. The Mini-Mental State Examination as a diagnostic and screening test for delirium: systematic review and meta- analysis. Gen Hosp Psychiatry 2014;36:627-33.
15. Muela HC, Costa-Hong VA, Yassuda MS, et al. Hypertension severity is associated with impaired cognitive performance. J Am Heart Assoc 2017;6:e004579.
16. Wu L, He Y, Jiang B, et al. The association between the prevalence, treatment and control of hypertension and the risk of mild cognitive impairment in an elderly urban population in China. Hypertens Res 2016;39:367-75.
17. Ballesteros Rozo S. Actores individuales y colectivos asociados con la prevalencia de limitaciones funcionales del adulto mayor en Colombia. Análisis multinivel Análisismultinivel. Universidad del Rosario, 2017.
18. Sharifi F, Hedayat M, Fakhrzadeh H, et al. Hypertension and cognitive impairment: Kahrizak elderly study. Int J Gerontol 2011;5:212-6.
19. Hashem HA, Mustafa YH. Correlation between Metabolic Syndrome and Mild Cognitive Impairment. J Alzheimers Park doi: 10.4172/2161-0460.1000414
20. He Q, Li Q, Zhao J, et al. Relationship between plasma lipids and mild cognitive impairment in the elderly Chinese: a case-control study. Lipids Health Dis 2016;15:146.
21. Koenig W, Sund M, Ernst E, et al. Association between rheology and components of lipoproteins in human blood. Results from the MONICA project. Circulation 1992;85:2197-204.
22. Yin ZX, Shi XM, Kraus VB, et al. High normal plasma triglycerides are associated with preserved cognitive function in Chinese oldest-old. Age Ageing 2012;41:600-6.
23. Gaidhane S, Gaidhane AM, Zahiruddin QS, et al. Essential hypertension and cognitive function in elderly. Glob. J. Med. Public Health 2012;3:1-12.
24. Okusaga O, Stewart MC, Butcher I, et al. Smoking, hypercholesterolaemia and hypertension as risk factors for cognitive impairment in older adults. Age Ageing 2013;42:306-11.
25. Tsivgoulis G, Alexandrov AV, Wadley VG, et al. Association of higher diastolic blood pressure levels with cognitive impairment. Neurology 2009;73:589-95.
26. Shah NS, Vidal JS, Masaki K, et al. Midlife blood pressure, plasma β-amyloid, and the risk for Alzheimer disease: the Honolulu Asia Aging Study. Hypertension 2012;59:780-6.
27. Faraci FM. Protecting against vascular disease in brain. Am J Physiol-Heart Circ Physiol 2011;300:H1566-82.
28. Poggesi A, Pasi M, Pescini F, et al. Circulating biologic markers of endothelial dysfunction in cerebral small vessel disease: a review. J Cereb Blood Flow Metab 2016;36:72-94.

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The Aortic Annulus, Sinus of Valsalva, Ascending Aorta and Z-score Values in Healthy Children

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Abstract

Objectives: The aim of this study is to evaluate echocardiographically (and determine pathology if there is any) the diameters and Z-scores of aortic annulus, sinus of valsalva and ascending aorta in healthy children.

Materials and Methods: This retrospective cross-sectional study includes seventy patients with no important hemodynamically congenital heart disease. Forty-one of 0-18 (average 5.69) year old patients are boys (58.6%) and 29 are girls (41.4%). Patients' height and weight values were assessed. Body surface area and Z-score values were calculated. Aortic annulus, sinus of valsalva and ascending aorta were measured on the parasternal long axis view. The indexed values were obtained by dividing all measured parameters by body surface area.

Results: Average indexed aortic annulus value is 22.77 mm/m^2; sinus of valsalva value is 30.51 mm/m^2 and ascending aortic value is 28.30 mm/m^2 in our study. Average aortic annulus value for nine patients whose Z-scores are >2 is 26.5 mm/m^2 ; sinus of valsalva value is 38.24 mm/m^2 and ascending aortic value is 34.94 mm/m^2.

Conclusion: In the present study, children aged between 0-18 years, mean aortic annulus, sinus of valsalva and ascending aorta, Z-scores and indexed values (aortic annulus/mm^2, sinus of valsalva/m^2, ascending aorta/m^2) were determined. In this study including few patients, aortic dilatations have been observed in the measurements of six of 67 patients (8.9%) who visited for the first time and 9 of 70 patients in total (12%). It is remarkable that nonsyndromic newborn and infant patients who are thought to be healthy have also various levels of aortic dilatations even before they were diagnosed with aortopathy.

Keywords: Aortopathy, aorta annulus, sinus of valsalva, ascending aorta, Z-score, children

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Introduction

Aortic pathologies like hypoplasia, dilatation, aneurysm and rupture at various levels of aorta, valvular stenosis/insufficiency and coronary arterial abnormalities can be seen in children and adults. These congenital and acquired pathologies can cause serious mortality and morbidity.

Primary aortic dilatation is mostly seen with conotruncal anomalies such as bicuspid aortic valve, CoA (coarctation of aorta), Tetralogy of Fallot, PA/VSD (Pulmonary atresia/Ventricular Septal Defect), and TA (Truncus arteriosus). This is also a feature in genetic syndromes such as Marfan, Loeys-Dietz, vascular Ehlers-Danlos, and Turner syndromes. Secondary dilatation of the aorta is seen after congenital cardiac surgery, as in the Ross, arterial switch operation, systemic outflow tract reconstruction in single-ventricle patients. Aortic pathology can be at a single level, as well as at multiple levels, in the entire aortic wall(1,2).

Objectives

The aim of this study is to echocardiographically evaluate (and determine pathology if there is any) the diameters and Z-scores of aortic annulus (Ao ann), sinus of valsalva (SoV) and ascending aorta (Asc ao) in healthy children.

Materials and Methods

Patients

This retrospective cross-sectional study included patients who were admitted to Pediatric Cardiology Department during the period from September 01 to October 24 in 2018. Patients with cardiac murmur, chest pain, fatigue, and palpitation were assessed with their medical histories, physical examination, ECG, and when needed, telecardiography. No sedation was applied to patients before echocardiography. This study includes 70 patients with no important hemodynamically congenital heart disease, out of 579 patients whose various levels of aortic diameters (Ao ann, SoV, Asc ao) were measured through echocardiography. Forty one of 0-18 (average 5.69) year-old patients were boys (58.6%) and 29 were girls (41.4%).Thirty one of them (44.3%) were 0-1-year-old, 39 of them (55.7%) were 1-18-year-old. Patients' height and weight values were assessed and BSA (Body surface area) and Z-score values were calculated. BSA was calculated through the formula of 4x+7/90+x, and Z-score values were obtained according to the report of Cantinotti et al.(3) Written informed consent for participation was obtained.

Echocardiography

Patients were assessed by the same researcher (SP) by using Philips HDXE11 Phase Array (Philips Medical System, Nederland BV, Best, the Netherlands) pediatric transducer with S8-3 and S4-2 mHz Broadband sector array transducers. Routine transthoracic echocardiographic examination was conducted according to the segmental analysis method. Aortic valve Doppler measurements were done in apical 4-chamber and suprasternal views. Ao ann, SoV and Asc ao measurements in consecutive cardiac beats were recorded as the average of three measurements. Ao ann was measured on the parasternal long axis view as the maximum distance between the hinge points of leaflets in the systole, and SoV and Asc ao were measured as perpendicular to the long axis of aorta and as forming maximum end diastolic diameters(4,5). The indexed values [indexed Ao ann (iAa); indexed SoV (iSoV); indexed Asc ao (iAsc ao)] were obtained by dividing all measured parameters by BSA.

Statistical Analysis

SPSS 15.0 (SPSS for Windows v.15.0; IBM-SPSS Inc., Chicago, IL, USA) software was used for all statistical analyses. An Independent Sample t-test was used for the comparison of parametric values. Pearson correlation test and linear regression analysis were applied to evaluate the correlation among variables. The correlation coefficient which was <0.3 was defined as weak; 0.3-0.7 as medium, and >0.7 as strong. Continuous variables were reported as mean ± SD (standard deviation).

As given in literature, the Z-score, a standardized value that indicates by how many SDs a value is above or below the mean in a normally distributed population, has been recommended for normalization. A measurement that is two SDs above the mean (the 97.7th percentile) has a Z-score of +2, whereas a measurement that is two SDs below the mean (the 2.3rd percentile) has a Z-score of -2[6].

Results

The basic characteristics and echocardiographic findings of all patients are presented in Table 1. Patients were categorized by BSA into five groups. BSA with 0.12-2.25 m^2 formed group 1, and 0.251-0.5 m^2 group 2, 0.51-1 m^2 group 3, 1.01-1.5 m^2 group 4, and 1.51-1.9 m^2 group 5. Z-score and indexed aortic measurements [IAM (iAa, iSoV, iAsc ao)] are given in Tables 2-4. It was found out that there was not any significant difference of Z-score values and IAM according to gender. There was a close correlation between BSA and Ao ann (r= 0.935, p<0.001).

Table 1. Anthropometrşc and echocardiographic features of patients

	Minimum	Maximum	Mean	SD
Age (year)	0.00	18.00	5.68	5.86
Weight (kg)	1.49	79.35	22.23	20.64
Height (cm)	38.00	179.00	102.36	46.65
BSA (m^2)	0.14	1.91	0.75	0.52
Z-score (weight)	-3.83	2.41	-0.15	1.39
Z-score (height)	-7.45	4.31	0.11	1.62
Aortic annulus (mm)	5.62	22.20	13.00	5.30
Sinus of valsalva (mm)	7.55	35.30	17.30	7.19
Ascending aorta (mm)	6.39	32.50	15.97	6.64
Z-score aortic annulus	-2.23	4.19	0.11	1.18
Z-score sinus of valsalva	-3.02	6.37	-0.28	1.51
Z-score ascending aorta	-3.92	4.53	0.10	1.36
Aortic annulus/m^2	10.17	41.66	22.77	8.80
Sinus of valsalva/m^2	13.21	61	30.51	12.33
Ascending aorta/m^2	12.40	58.88	28.30	11.92

SD: Standard deviation, BSA: Body surface area

The same close correlation was also seen between BSA -SoV (r=0.886, p<0.001) and BSA-Asc ao (r=0.921, p<0.001). Similarly, close correlations were found between BSA-iAa (r=0.82, p<0.001), BSA-iSoV (r=0.78, p<0.001) and BSA-iAsc ao (r=0.74, p<0.001).

Anthropometric measurements of patients were evaluated with the "Standardized Height and Weight calculator", and Z-scores of height and weight values were obtained. There was a medium and statistically meaningful correlation between z-scores of height and weight (r=0.67, p<0.001).

There was a statistically significant and strong correlation between Z-scores of Ao ann and SoV (r=0.778, p<0.001). It was found out that there was a statistically meaningful and medium correlation between Z-scores of Ao ann and Asc ao (r=0.427, p<0.001). A statistically significant and medium correlation between Z-scores of SoV and Asc ao (r=0.644, p<0.001) were identified. A statistically significant and highly strong correlation was revealed between Ao ann and Asc Ao; the same correlation was found out between SoV and Asc ao (r=0.949, p<0.001).

There was a statistically significant and similar strong correlation between Ao ann and SoV (r=0.972, p<0,001). Z-score values of the three patients, whose z-score Ao ann values were greater than 2 (>2), were 2.98, 2.8 and 4.19. Echocardiography of one of the patients was normal. The second patient had scoliosis, MVP (Mitral valve prolapse) and AVP (aortic valve prolapse). The third patient had scoliosis, MVP, AVP, phenotypic Marfan syndrome. No genetic pathologies were detected.

Z-scores of the three patients, whose Z-scores of SoV values were greater than 2 (>2), were 3.17, 2.09 and 6.37. One of the patients had hemodynamically insignificant small VSD. The other two were the patients with scoliosis, whose Z-scores of annulus values were greater than 2 (>2).

There were six patients whose Z-score of asc ao was greater than 2 (>2). One of them, whose SoV was greater than 2 (>2), had small VSD with Z-scores. That patient's Z-score value was 4.53. The Z-scores of Asc ao values of the others were 2.18, 2.3, 2.48, 2.67, and 2.73. The patients whose Z-score of Asc ao values were 2.48 and 2.3 were a 1.5-month-old girl and 3-month-old boy. The other echocardiographic findings of those patients were normal. A 17.5-year-old boy and, a 18- year-old girl were two patients with no congenital heart disease, and no pathology was associated with echocardiography except for that Z-score of Asc ao was greater than 2 (>2). Their values were 2.73 and 2.18, respectively. All these values were summarized in Table 5.

Table 2. Z-score values according to BSA

			Z-score annulus	Z-score sinus of valsalva	Z-score of ascend aorta
BSA (m^2)	**Group**	**n (%)**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
0-0.25	1	22 (31.46)	-0.42±1.27	-1.01±1.36	-0.4±1.48
0.251-0.5	2	9 (12.9)	0.18±0.61	-0.57±0.99	-0.62±0.83
0.51-1	3	15 (21.4)	0.92±1.34	0.78±2.02	0.76±1.43
1.01-1.5	4	9 (12.9)	-0.28±0.86	-0.61±0.98	0.49±1.44
1.51-1.9	5	15 (21.4)	0.21±0.84	0.11±1	0.36±0.84
	Total	70	0.11±1.18	-0.28±1.51	0.09±1.35

SD: Standard deviation, BSA: Body surface area

Table 3. Aortic annulus, sinus of valsalva and ascending aorta values

			Aort annulus (mm)	Sinus of valsalva (mm)	Asc Ao (mm)
BSA (m^2)	**Group**	**n (%)**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
0-0.25	1	22 (31.46)	6.89±0.91	9.27±1.18	8.78±1.15
0.251-0.5	2	9 (12.9)	9.23±1.08	1.21±1.63	10.76±1.33
0.51-1	3	15 (21.4)	15.43±2.47	20.98±4.84	18.73±2.77
1.01-1.5	4	9 (12.9)	17.54±0.87	23.41±2.22	21.43±2.5
1.51-1.9	5	15 (21.4)	20.08±1.54	25.83±2.36	25.09±3.76
	Total	70	13±5.3	17.3±7.19	15.97±6.64

SD: Standard deviation, BSA: Body surface area, Asc Ao: Ascending aorta

Table 4. Indexed aortic measurements

			Aort annulus/m^2	Sinus of valsalva/m^2	Asc Ao/m^2
BSA (m^2)	**Group**	**n (%)**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
0-0.25	1	22 (31.46)	33.06±4.7	44.61±7.14	42.37±7.81
0.251-0.5	2	9 (12.9)	26.97±2.88	35.3±3.89	31.44±3.66
0.51-1	3	15 (21.4)	19.59±2.94	26.79±6.59	24.12±5.56
1.01-1.5	4	9 (12.9)	12±1.12	15.43±1.69	14.99±2.42
1.51-1.9	5	15 (21.4)	14.8±1.77	19.72±2.54	17.96±1.78
	Total	70	22.77±8.8	30.51±12.33	28.3±11.92

SD: Standard deviation, BSA: Body surface area, Asc Ao: Ascending aorta

Table 5. Patients with Z-score >2

Patients	Age (year)	Sex	Z-score Ao ann	Z-score SoV	Z-score Asc ao
EC	6.00	Female	2.80	-	-
BYK	6.50	Male	4.19	6.37	2.67
YAD	6.00	Male	-	3.17	4.53
CPB	7.75	Male	-	2.09	-
NU	18.00	Female	-	-	2.18
YA	17.50	Male	-	-	2.73
FI	0.04	Female	2.98	-	-
PA	0.01	Female	-	-	2.48
KIS	0.02	Male	-	-	2.30

Ao ann: Aortic annulus, SoV: Sinus of valsalva, Asc ao: Ascending aorta

Discussion

As aort pathologies can be seen with isolated or complicated heart diseases in children, they can also accompany vasculitis (like Takayashu arteritis, Kawasaki disease, Behçet's disease) and genetic connective tissue disorders (Vascular form of Ehlers-Danlos, Marfan sydrome and Tuberous sclerosis). It has made us review the importance of the situation due to the significant mortality and morbidity seen in the influenced individuals. It is estimated that the frequency of aneurysm is 5.9/100000 patients per year in adults. Although it is estimated that the frequency is lower in children, there are no data for that[7,8].

Cantinotti et al.[3] have performed 2D echocardiography and annulus and vascular diameter measurements in their study conducted on 1151 healthy Caucasian Italian children with the mean age of 23 months and with BSA 0.54 m^2. In our study, the mean age was 5.68 years and BSA was 0.75 m^2 [3].

In Cantinotti et al.[3]'s nomograms, the mean Ao ann was 13.48 mm, SoV was 18.4 mm and Asc ao was 16.6 mm according to the BSA of 0.75 m^2. These values were measured as 13 mm, 17.3 mm and 15.97 mm, respectively, in our study. These were similar to the values that Cantinotti et al.[3] reported.

With an average Ao ann Z-score value of 0.11 for the mean BSA value of 0.75 m^2, nomogram Ao ann value determined by Cantinotti et al.[3] was 13.5 mm while it was 13 mm in our study. Similarly, with an average SoV Z-score value of 0.28 for the mean BSA value of 0.75 m^2, nomogram SoV value determined by Cantinotti et al.[3] was 16.66 mm while it was 17.3 mm in our study.

As the findings above, with an average Asc Ao Z-score value of 0.10 for the mean BSA value of 0.75 m^2, nomogram Asc Ao Z-score value reported by Cantinotti et al. [3] was 17 mm while it was 15.97 mm in our study.

The mean gestational age was 29.8 weeks, weight was 1479 g, BSA was 0.13 m^2 in the study of Abushaban et al.[9], in which they reported reference intervals for aortic diameter in preterm infants[9]. Asc Ao diameter for the mean BSA value was 7.5 mm. This value is also in accordance with the mean aortic diameter value of 8.78 mm in patients in group 1. There was a 34-35-week-old patient with intrauterin growth retardation in our study. While Z-score Asc Ao value given for the mean BSA value of 0.13 m^2 was between-1.79 and +1.37, the mean Asc Ao Z-score value for group 1 was -0.40 in our study.

Kervancioglu et al.[10] assessed aortic root diameter in 229 healthy children through M-mode echocardiography. They reported that the mean aortic root diameter was 14.8 mm and the mean indexed aortic root diameter was 19.9 mm/m^2.

It is known that indexed diameter is (diameter/BSA) also important just like the diameter of aortic segment in normal children and adults. The maximum level of the indexed aortic root is >21 mm/m^2; significant dilatation >25 mm/m^2; meaningful risk for rupture >27.5 mm/m^2[11,12]. Z-score value defined for mild aortic dilatation is 1.9-3 and 3-4 for moderate dilatation[13].

Chong et al.[14] studied on 67 children with operated Tetralogy of Fallot whose mean age was 8.3±5.6 years. They reported the prevalence of aortic dilatation (Z-score >2) as 88% for aortic annulus, 87% for sinus of valsalva, 61% for sinotubular junction, and 63% for ascending aorta.

In our study, the mean indexed ao annulus value was 22.77 mm/m^2, sinus of valsalva value was 30.51 mm/m^2, and ascending aortic value was 28.30 mm/m^2.

Three of nine patients with Z-score values of >2 were the patients who were diagnosed, followed-up, and treated previously. Six of them were the patients who were assessed echocardiographically for the first time. The mean aortic annulus value for nine patients whose Z-scores were >2 was 26.5 mm/m^2, sinus of valsalva value was 38.24 mm/m^2, and ascending aortic value was 34.94 mm/m^2. Two of the patients with Z-scores >3 were diagnosed previously. Z-score aortic annulus and sinus of valsalva values for a 6.5-year-old boy patient were 4.19 and 6.37, respectively. Z-score SoV and ascending aortic values for a 6-year- old boy patient were 3.17 and 4.53, respectively. Seven patients with Z-scores between 2 and 3 were first time visiting patients.

Conclusion

In the present study, children aged between 0 and 18 years, the mean aortic annulus, sinus of valsalva and ascending aorta, Z-scores and indexed values (aortic annulus/mm^2, sinus of valsalva/m^2, ascending aorta/m^2) were determined.

In this cross-sectional study including a few patients, aortic dilatations were observed in the measurements of six of 67 patients (8.9%) who visited for the first time and in nine of 70 patients in total (12%).

It is remarkable that non-syndromic newborn and infant patients who are thought to be healthy have also various levels of aortic dilatations even before they are diagnosed with aortopathy. We believe that the findings and results obtained in this cross-sectional study will lead to larger studies with patients with/without congenital heart diseases and syndromic/non-syndromic patients.

Ethics

Ethics Committee Approval: The center where I worked was changed (Merkezefendi State Hospital to Manisa City Hospital) one week after the end of the study. Ethics committee approval could not be obtained because these institutions were not educational and research hospitals.

Informed Consent: Informed consent was taken from the patients.

Peer-review: Externally and internally peer-reviewed.

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References

1. Francois K. Aortopathy associated with congenital heart disease: A current literature review. Ann Pediatr Cardiol 2015;8:25-36.
2. Zanjani KS, Niwa K. Aortic dilatation and aortopathy in congenital heart disease. J Cardiol 2013;61:16-21.
3. Cantinotti M, Giordano R, Scalese M, et al. Nomograms for two-dimensional echocardiography derived valvular and arterial dimensions in Caucasian children. J Cardiol 2017;69:208-15.
4. Lai WW, Gewa T, Shirali GS, et al. Guidelines and standards for performance of a pediatric echocardiogram: A report from the Task Force of the Pediatric Council of the American Society of Echocardiography. J Am Soc Echocardiogr 2006;19:1413-30.
5. Lopez L, Colan SD, Frommelt PC, et al. Guidelines and Standards Recommendation for Quantification Methods During the Performance of a Pediatric Echocardiogram: A Report From the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. J Am Soc Echocardiogr 2010;23:465-95.
6. Colan SD. The way and how of Z scores. J Am Soc Echocardiogr 2013;26:38-40.
7. Bickerstaff LK, Pairolero PC, Hollier LH, et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982;92:1103-8.
8. Puranik R, Chow CK, Duflou JA, et al. Sudden death in the young. Heart Rhythm 2005;2:1277-82.
9. Abushaban L, Mariappa TV, Rathinasamy J, et al. Normal reference for aortic diameters in preterm infants. J Saudi Heart Assoc 2018;30:86-94.
10. Kervancioglu P, Kervancioglu M, Tuncer CM. Echocardiographic study of aortic root diameter in healthy children. Saudi Med J 2006;27:27-30.
11. Roman MJ, Devereux RB, Kramer-Fox R, et al. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. Am J Cardiol 1989;64:507-12.
12. Davies RR, Gallo A, Coady MA, et al. Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. Ann Thorac Surg 2006;81:169-77.
13. Lang RM, Bierig M, Devereux RB, et al. Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committe; European Association of Echocardiography. Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber

Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440-63.

14. Chong Wy, Wong WHS, Chiu CSW, Cheung YF. Aortic Root Dilation and Aortic Elastic Properties in Children After Repair of Tetralogy of Fallot. Am J Cardiol 2006; 97:905-9.

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The Relationship Among Fasting Blood Glucose, Lipid Panel, and Global Scoring of Myocardial Perfusion Imaging

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Abstract

Objectives: This study aimed to evaluate the impact of fasting blood glucose and lipid panel values on the scores in myocardial perfusion scintigraphy (MPS) and the percentage of perfusion defects.

Materials and Methods: Medical data of 1120 consecutive patients were reviewed. The fasting blood glucose and lipid panel values within ±30 days from MPS imaging were considered. A total of 274 (24%) patients (125 female, 149 male) were included in the study. Summed stress score (SSS), summed rest score, summed difference score (SDS), stress total perfusion defect (TPD), rest TPD, and difference TPD values were obtained by using a semi-quantitative (17 segment model, 5-point scoring) method. The ejection fraction (EF) was measured via the MPS images that synchronized with an electrocardiogram. Fasting blood glucose, lipid profile, ejection fraction, gender, and the presence of coronary artery disease were compared to MPS scores and TPD percentages by using the t-test. A logistic regression test was used to detect the parameters that might cause abnormal SSS and SDS scores.

Results: Perfusion defects (SSS>3) were observed in 196 (72%) patients. In 172 (63%) of these patients, there was a reversible perfusion defect (SDS>2). During MPS imaging, decreased HDL (<40 mg/dL) and increased fasting blood glucose (>125 mg/dL) levels in all patients, elevated triglyceride (>200 mg/dL) values in the coronary

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Abstract

artery disease (CAD) + group, high total cholesterol (>200 mg/dL) and decreased HDL (<40 mg/dL) levels in the non-CAD group were the factors that were found to have statistically significant association with higher global scores. Independently from the fasting blood glucose and lipid profile, impaired EF values (<50%) and male gender led to significantly higher global scores. While EF value and male gender were determined as independent factors for abnormal SSS, triglyceride and female gender were found to be in association with abnormal SDS.

Conclusion: This study emphasises that fasting blood glucose, lipid profile, gender, and EF values may be used as a beneficial tool to predict the MPS global scores and perfusion defect rates.

Keywords: Myocardial perfusion scintigraphy, global scoring, SSS, SDS, TPD

Introduction

Single-photon emission computed tomography (SPECT) and imaging of myocardial perfusion scintigraphy (MPS) with radiotracers are widely used in order to establish the diagnosis, to assess the risk and treatment management, and to evaluate treatment response of coronary artery disease[1]. In the evaluation of the MPS, visual and automatically calculated 17 segments, 5-points scoring evaluation methods are frequently utilized. Thus, the prevalence and severity of perfusion anomaly can be indicated by a single semi-quantitative measurement[2]. Basically, in MPS, two different images identified as stress and rest are evaluated. In stress images, the total of scores in all 17 segments are entitled as summed stress score (SSS), similarly, the overall score in rest images are entitled as summed rest score (SRS). The difference between these scores constitutes the summed difference score (SDS)[3]. Furthermore, total perfusion defect percentage (stress TPD) of the left ventricular mass in the stress images and total perfusion defect percentage (rest TPD) of the left ventricular mass in rest images can be obtained from the program. The difference between these two values constitutes the difference TPD. SDS and difference TPD are in association with reversible defect. In case of the difference TPD ≥10, an emergent coronary angiography is suggested for revascularization[4,5].

Diabetes is a well-known risk factor for coronary artery disease for over decades[6]. It is known that microvascular and macrovascular dysfunction gradually develop in patients with high blood glucose levels[7]. On the other hand, elevated cholesterol levels cause endothelial dysfunction hence lead to ischemic heart disease[8]. Dysfunction areas in vessels that occur secondary to impaired glucose and lipid parameters can be detected via MPS images.

This study aimed to determine the effects of fasting blood glucose and lipid panel [total cholesterol, triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL)] values on the perfusion defect percentages and scoring systems in myocardial perfusion scintigraphy.

Materials and Methods

The hospital records of overall 1120 consecutive enrollees who underwent myocardial perfusion scintigraphy with the suspect/diagnosis of coronary artery disease between July 2018 and April 2019 were retrospectively reviewed. Six hundred and ninety nine patients who had no biochemical tests in 30 days before or after the MPS and 140 patients without rest images were excluded from the study. The process of six patients could not be performed optimally due to gastrointestinal system activity. In addition to these, one patient was excluded for the reason that electrogram syncranized (GATED) image was not possible to obtain due to arrhythmia. Consequently, 274 patients were included. This study was approved by the Local Ethical Committee.

All patients who underwent both stress and rest myocardial perfusion scintigraphy and had fasting blood glucose and lipid profile (total cholesterol, triglyceride, HDL, LDL) within ±30 days from the MPS date were included in the study.

On the other hand, the patients who had no fasting blood glucose and lipid profile analyses within the first 30 days before or after the MPS in the hospital database were excluded. Besides, the patients without resting MPS or GATED imaging and the patients with failed optimal image processing due to the physiological radiopharmaceutical uptake in the gastrointestinal tract were excluded from the study.

The patients were informed about the imaging process and possible complications: thereafter, an informed consent form was obtained from each patient. The medications with beta-blockers, calcium channel blockers, and long-acting nitrates were discontinued for 48 hours before imaging. Patients were informed concerning they should not drink tea or coffee in the last 24 hours and avoid food and fluid intake for the last 4 hours.

An anamnesis was taken and blood pressure was measured in imaging day. Then, a nuclear medicine physician evaluated the choice of stress test method regarding whether to apply pharmacologically or by effort. A single day (stress-rest) protocol was performed to all patients. The rest imaging was not performed on patients in the absence of any defect or suspicious lesion visually.

The treadmill exercise test was applied to the patients who were planned to undergo stress test by effort. The targeted heart rate (220-age) was calculated according to the Bruce/modified Bruce protocol. Then 9 mCi Tc-99m MIBI injection was administered to the patients who reached 85% of the targeted heart rate. Patients were expected to reach 100% of the targeted heart rate following injection. The protocol was continued for at least 1 minute for those who failed to reach 100% of the targeted heart rate.

Adenosine was used in an attempt to establish pharmacological stress if there was no contraindication. The patients were monitorized and then intravenous adenosine infusion was initiated with the dosage of 140 mcg/kg/m. In the third minute of the infusion, 9 mCi MIBI injection was administered. Thereafter, the adenosine infusion was continued for three minutes and the test was terminated. Imaging was performed on all stress test applied patients 30-45 minutes after Tc-99m MIBI injection.

The SPECT images were obtained by using GATED, Mediso AnyScan dual-head gamma camera (Mediso AnyScan, Hungary) with 64x64 matrix, 140-keV peak, 20% energy window, step&shot technique (25 seconds), high-resolution parallel-hole collimators to acquire 32×40-s projections along a 180°, non-circular orbit with heads at 90° from another. Raw images were filtered by using a Butterworth back projection.

After 3 hours of radiopharmaceutical injection during the stress test, 23 mCi Tc-99m MIBI injection was performed in resting patients. Then, the rest MPS images of the patients were obtained with the same imaging protocol 45-60 minutes after injection.

Imaging Analysis and Evaluation of Biochemical Parameters

Imaging analysis was performed by an experienced nuclear medicine physician. To determine the ejection fraction, Cedar's Sinai Quantitative GATED SPECT and, for ischemia scores, Cedar's Sinai Quantitative Perfusion SPECT package program were used. Ejection fraction was determined with GATED images. In ischemia scoring, left ventricle myocardium was separated into 17 segments and each was scored from 0 to 4 (Table 1). SSS, SRS, SDS, stress TPD, and rest TPD measurements were obtained by using the program. However, the percentage of total perfusion defect (difference TPD) between rest and perfusion images was calculated manually.

The high SRS and rest TPD values were evaluated as a fixed defect (infarct) because of demonstrating the presence of a defect in resting myocardium. On the other hand, high SDS and difference TPD values were defined as a reversible defect to express the recovery in rest images, which was found previously in stress images. SSS>3 and SDS>2 values were considered as abnormal[3,9].

The cut off values were set as: fasting blood glucose 125 mg/dL, total cholesterol and triglyceride 200 mg/dL, HDL 40 mg/dL, LDL 130 mg/dL[10].

Statistical Analysis

The acquired data were evaluated by using IBM SPSS 22 (Armonk, NY) package program. The mean values and range were used for variables. Biochemical parameters, ejection fraction (EF), gender in all patients, patients with coronary artery disease (CAD) and those with no diagnosis of CAD; the results of left ventricular myocardium scores and perfusion defects were compared. The Student's t-test was used in pairwise comparisons. The binary logistic regression test was used to figure out the parameters affecting abnormal SSS and SDS values. A p value of <0.05 was considered as statistically significant.

Results

The mean age of 274 patients (125 female, 149 male) was 62±11 years. During imaging, 99 patients (36%) had a diagnosis of CAD confirmed by coronary angiography. Sixty-four (65%) of patients had a history of stent, 22 (22%) had a history of by-pass, and five (5%) had a history of by-pass + stent. Eight (8%) patients were on medical follow up. Besides, 72 (26%) patients had diabetes mellitus, 21 (8%) of whom were under insulin treatment.

All Patients

Abnormal SSS and SDS values were observed in 196 (72%) and 172 (63%) patients respectively. SDS value was severely high (≥7) in 60 patients. Meanwhile, in 36 (13%) patients, difference TDP was ≥10%. There were significant differences among fasting blood glucose, HDL, EF, the presence of CAD, gender, and some MPS scores. These outcomes were presented in Table 2. In patients with fasting blood glucose above 125 mg/dL, reversible defect was more frequent. When there were more fixed defects in patients with HDL value of <40 mg/dL, reversible defects were more common in the individuals with ≥40 mg/dL HDL levels. The patients with EF <50% and CAD+, the fixed defect percentage was significantly higher. While more fixed defects were observed in males, reversible defects were more common in females. However, there was no statistically significant difference among total cholesterol, triglyceride, LDL levels and global scores, and TPD values. EF value (Wald=6.063, HR=1.037 (95% Cl=1.007-1.067), p=0.014) and male gender (Wald=8.592, HR=2.257 (95% Cl=1.310-3.890), p=0.003) were found to be independent factors to predict abnormal SSS. Triglyceride level (Wald=5.102, HR=1.004 (95% Cl=1.001-1.007), p=0.024) and female gender (Wald=16.981, HR=3.021 (95% Cl=1.786-5.112), p<0.001) were determined as independent predictors to detect abnormal SDS.

Table 1. Five-point scale

Point	Meaning
0	Normal
1	Slightly reduction uptake
2	Moderate reduction uptake
3	Severe reduction uptake
4	Absent of uptake

CAD+ Group

There were abnormal SSS and SDS values in 78 (79%) and 66 (67%) respectively. SDS value was ≥7 in 24 (24%) patients. Therewithal, in 15 (15%) patients, the difference TPD was ≥10%. Table 3 presents the results during MPS imaging regarding CAD+ patients. CAD+ and triglyceride >200 mg/dL patients had more fixed defects, when compared to triglyceride ≤200 mg/dL ones. Nonetheless, the frequency of fixed defects was higher in patients with EF<50 either. In the CAD+ group, reversible defects were more common in females rather than males. Although more fixed defects were observed in males, this difference was not statistically significant. In CAD+ patients, there was no difference among fasting blood glucose, total cholesterol, LDL, HDL levels and MPS scores or TPD percentages. Female gender was found to be an independent predictor for the detection of abnormal SDS in this group (Wald=4.390, HR=2.778 (95% Cl=1.068-7.224), p=0.036).

Suspicious CAD+ Group

In this group, SSS in 118 (67%) and SDS in 106 (61%) patients were abnormal. In 36 (21%) patients, SDS values were ≥7 and 21 (12%) patients had difference TPD values greater than or equal to 10%. In Table 4, the results of the non-CAD diagnosed patients during MPS images are presented. There were more observed reversible defects in total cholesterol >200 mg/dL subgroup in this cohort. In patients with HDL <40 mg/dL and EF<50, the fixed defect rate was higher while the reversible defects were more common in patients with HDL ≥40 mg/dL. In the non-CAD (suspected CAD) group, male patients had less fixed defects while more reversible defects were observed in females. However, there was no significant difference in comparisons among fasting blood glucose, triglyceride, LDL levels and MPS scores, TPD percentages, in this group.

Table 2. Global scores of all patients according to fasting blood glucose, lipid profile, EF, CAD, and gender

	n	SSS	SRS	SDS	Stress TPD (%)	Rest TPD (%)	Difference TPD (%)
Total	274	7.8±7.1	3.7±6.2	4.2±3.2	8.9±9.2	3.7±7.9	5.2±3.7
Glucose							
≤125 mg/dL	192	7.6±7.0	3.7±6.2	3.9±3.2	8.6±9.4	3.7±7.7	4.9±3.8
>125 mg/dL	82	8.5±7.0	3.7±6.5	4.8±3.2	9.6±8.9	3.8±8.5	5.8±3.7
p value		**0.307**	**0.963**	**0.034***	**0.426**	**0.917**	**0.082**
Total cholesterol							
≤200 mg/dL	135	8.3±7.8	4.4±6.9	3.9±3.2	9.6+10.1	4.4±8.7	5.2±4.0
>200 mg/dL	139	7.4±6.2	3.1±5.5	4.4±3.1	8.2±8.2	3.1±7.1	5.1±3.6
p value		**0.324**	**0.094**	**0.260**	**0.215**	**0.168**	**0.902**
Triglyceride							
≤200 mg/dL	218	7.6±6.5	3.5±5.8	4.2±3.1	8.6±8.5	3.4±7.3	5.2±3.7
>200 mg/dL	56	8.8±8.9	4.7±7.6	4.1±3.5	10.3±11.7	5.2±9.9	5.1±4.1
p value		**0.368**	**0.275**	**0.881**	**0.295**	**0.204**	**0.931**
HDL							
<40 mg/dL	92	8.8±7.8	5.2±7.2	3.6±2.8	10.4±10.4	5.4±8.8	5.0±3.3
≥40 mg/dL	182	7.4±6.6	3.0±5.6	4.4±3.3	8.2±8.5	2.9±7.4	5.2±4.0
p value		**0.129**	**0.010***	**0.047***	**0.079**	**0.024***	**0.198**
LDL							
≤130 mg/dL	146	8.0±7.4	4.0±6.4	4.0±3.3	9.3±9.6	4.0±8.2	5.2±4.0
>130 mg/dL	128	7.6±6.6	3.4±6.1	4.3±3.0	8.5±8.7	3.4±7.6	5.1±3.5
p value		**0.614**	**0.394**	**0.561**	**0.473**	**0.504**	**0.724**
EF							
<50%	42	15.6±10.4	11.9±9.9	3.8±3.1	19.5±14.1	14.2±13.4	5.4±3.8
≥50%	232	6.4±5.1	2.2±3.7	4.2±3.2	7.0±6.4	1.9±4.4	5.1±3.8
p value		**<0.001***	**<0.001***	**0.457**	**<0.001***	**<0.001***	**0.719**
CAD							
Positive	99	10.6±9.1	6.2±8.2	4.4±3.6	12.6±12.1	6.9±10.8	5.7±4.2
Negative	175	6.3±5.0	2.3±4.2	4.0±3.0	6.8±6.3	2.0±4.9	4.9±3.4
p value		**<0.001***	**<0.001***	**0.333**	**<0.001***	**<0.001***	**0.078**
Gender							
Female	125	7.9±5.8	2.4±4.1	5.5±3.6	8.7±7.4	2.3±5.0	6.4±4.2
Male	149	7.7±8.0	4.8±7.4	3.0±2.3	9.0±10.5	4.9±9.6	4.1±3.0
p value		**0.847**	**0.001***	**<0.001***	**0.775**	**0.005***	**<0.001***

n: Number of the patients, SSS=Summed stress score, SRS: Summed rest score, SDS: Summed difference score, TPD: Total perfusion defect, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, CAD: Coronary artery disease, EF: Ejection fraction

Table 3. CAD positive patients global scoring

	n	SSS	SRS	SDS	Stress TPD (%)	Rest TPD (%)	Difference TPD (%)
Total	99	10.6±9.1	6.2±8.2	4.4±3.4	12.6±12.0	6.9±10.8	5.7±4.2
Glucose							
≤125 mg/dL	66	10.4±9.7	6.3±8.4	4.1±3.6	12.5±12.9	7.0±11.0	5.5±4.5
>125 mg/dL	33	10.9±7.8	5.9±7.9	5.0±3.1	12.7±10.2	6.6±10.7	6.1±3.7
p value		**0.768**	**0.830**	**0.218**	**0.949**	**0.840**	**0.484**
Total cholesterol							
≤200 mg/dL	62	10.9±9.6	6.3±8.4	4.6±3.7	13.2±12.6	7.0±11.0	6.2±4.7
>200 mg/dL	37	10.0±8.3	6.0±8.0	4.1±2.9	11.5±11.1	6.7±10.6	4.9±3.3
p value		**0.657**	**0.839**	**0.567**	**0.521**	**0.882**	**0.145**
Triglyceride							
≤200 mg/dL	79	9.4±8.2	5.2±7.5	4.3±3.4	11.0±11.0	5.6±9.8	5.5±4.3
>200 mg/dL	20	15.0±11.0	10.3±9.7	4.7±3.6	18.6±14.4	12.0±13.3	6.6±3.9
p value		**0.047***	**0.036***	**0.712**	**0.039***	**0.053**	**0.316**
HDL							
<40 mg/dL	38	11.9±9.0	7.7±8.6	4.3±3.2	14.6±12.4	8.7±10.8	5.9±3.5
≥40 mg/dL	61	9.7±9.1	5.2±7.9	4.5±3.6	11.3±11.8	5.7±10.8	5.6±4.6
p value		**0.239**	**0.141**	**0.768**	**0.189**	**0.187**	**0.716**
LDL							
≤130 mg/dL	62	10.3±9.2	5.7±7.8	4.7±3.8	12.3±12.0	6.0±4.6	6.0±4.6
>130 mg/dL	37	10.9±9.0	7.0±9.0	4.0±2.8	12.9±12.3	7.7±11.3	5.2±3.5
p value		**0.760**	**0.438**	**0.351**	**0.818**	**0.527**	**0.335**
EF							
<50%	22	20.2±10.9	16.2±9.8	4.1±3.8	25.8±14.8	20.1±13.5	5.7±4.6
≥50%	77	7.8±6.2	3.3±4.9	4.5±3.4	8.8±7.9	3.1±5.9	5.7±4.2
p value		**<0.001***	**<0.001***	**0.694**	**<0.001***	**<0.001***	**0.985**
Gender							
Female	38	10.6±7.3	4.5±5.5	6.2±3.8	12.5±9.7	4.8±7.2	7.6±5.0
Male	61	10.5±10.1	7.3±9.4	3.3±2.7	12.6±13.4	8.1±12.5	4.5±3.3
p value		**0.948**	**0.066**	**<0.001***	**0.944**	**0.102**	**0.001***

n: Number of the patients, SSS=Summed stress score, SRS: Summed rest score, SDS: Summed difference score, TPD: Total perfusion defect, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, CAD: Coronary artery disease, EF: Ejection fraction

Discussion

In our study, abnormal SSS and SDS were observed in 196 (72%) and 172 (63%) patients, respectively. Higher global scores were observed in patients with elevated HDL and fasting blood glucose levels. Furthermore, CAD+ patients with high triglyceride and CAD-patients with high total cholesterol and HDL levels were also found to be associated with high global scores, either. Independently from the fasting blood glucose and lipid profile, the presence of more fixed defects was observed in patients with impaired EF (<50%) and male gender. On the other hand, reversible defect frequency was higher in the female gender.

Diabetes is a well-known risk factor for CAD[11,12]. Beyond that, more cardiovascular event occurrence is reported with elevating blood glucose levels[13]. Furthermore, Ghatak et al.[14] documented that diabetic patients had higher SSS when compared to non-diabetic patients and consequently development of cardiac event was more common in this group. On the contrary, there was no significant difference between diabetic and non-diabetic populations in terms of SSS in our study. However, SDS was observed to be statistically higher in patients with fasting blood glucose >125 mg/dL. This circumstance may be interpreted in favor of that the diabetic patients have more reversible defects.

Table 4. CAD negative patients global scoring

	n	SSS	SRS	SDS	Stress TPD (%)	Rest TPD (%)	Difference TPD (%)
Total	175	6.3±5.0	2.3±4.2	4.0±3.0	6.8±6.3	2.0±4.9	4.9±3.4
Glucose							
≤125 mg/dL	129	6.3±5.2	2.5±4.4	3.8±2.9	6.8±6.6	2.2±5.1	4.6±3.4
>125 mg/dL	46	6.3±4.6	1.8±3.8	4.5±3.2	6.9±5.4	1.4±4.2	5.5±3.6
p value		**0.957**	**0.358**	**0.178**	**0.992**	**0.328**	**0.159**
Total cholesterol							
≤200 mg/dL	102	6.0±5.1	2.7±4.7	3.4±2.7	6.6±6.1	2.2±5.2	4.4±3.1
>200 mg/dL	73	6.5±5.0	2.0±3.8	4.4±3.2	7.0±6.4	1.8±4.7	5.2±3.6
p value		**0.429**	**0.323**	**0.024***	**0.658**	**0.560**	**0.100**
Triglyceride							
≤200 mg/dL	139	6.6±5.0	2.5±4.4	4.1±2.9	7.1±6.2	2.1±5.1	5.0±3.3
>200 mg/dL	36	5.3±5.1	1.5±3.5	3.8±3.4	5.7±6.6	1.4±4.0	4.3±4.0
p value		**0.187**	**0.221**	**0.613**	**0.234**	**0.420**	**0.302**
HDL							
<40 mg/dL	54	6.6±6.0	3.4±5.4	3.2±2.4	7.4±7.6	3.0±6.0	4.4±3.0
≥40 mg/dL	121	6.2±4.6	1.8±3.5	4.4±3.2	6.6±5.7	1.5±4.2	5.1±3.6
p value		**0.598**	**0.022***	**0.009***	**0.414**	**0.107**	**0.263**
LDL							
≤130 mg/dL	84	6.3±5.3	2.8±4.8	3.6±2.9	7.0±6.6	2.4±5.3	4.7±3.4
>130 mg/dL	91	6.3±4.8	1.9±3.6	4.4±3.1	6.7±6.0	1.6±4.5	5.0±3.5
p value		**0.916**	**0.167**	**0.084**	**0.712**	**0.325**	**0.471**
EF							
<50%	20	10.6±7.2	7.3±8.0	3.5±2.0	12.6±9.6	7.6±10.0	5.0±2.8
≥50%	155	5.7±4.4	1.7±2.9	4.1±3.1	6.1±5.4	1.3±3.2	4.9±3.5
p value		**0.008***	**0.006***	**0.237**	**0.007***	**0.011***	**0.851**
Gender							
Female	87	6.7±4.6	1.5±3.0	5.2±3.4	7.1±5.6	1.3±3.2	5.9±3.8
Male	88	5.9±5.4	3.1±5.1	2.8±2.0	6.6±7.0	2.7±6.1	3.9±2.7
p value		**0.246**	**0.018***	**<0.001***	**0.568**	**0.051**	**<0.001***

n: Number of the patients, SSS=Summed stress score, SRS: Summed rest score, SDS: Summed difference score, TPD: Total perfusion defect, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, CAD: Coronary artery disease, EF: Ejection fraction

In a study including the patients with SSS>4, diabetic patients had SSS=13.9±11.3, SDS=7.4±1.2[15]. However, our study included all diabetic patients regardless of SSS; therefore, SSS and SDS were lower as expected.

Several articles in the literature have specified SSS, SDS, hyperlipidemia, serum creatinine level, gender, and EF value as independent predictive factors for the detection of cardiac event development[16,17]. Similarly, impaired EF and male gender were found to be in correlation with elevated SSS while triglyceride levels and female gender were in correlation with SDS. Considering that elevated SSS and SDS are associated with increased cardiac events, our results are compatible with the current literature.

Another study calculated SSS, SRS, and SDS values as 13.3±6.0, 5.0±4.1, and 8.3±4.6, respectively, in patients with known CAD and not receiving statin therapy despite dyslipidemia[18]. The fact that the patients receiving statin therapy were excluded from the study suggests that only the patients with the diagnosis of new-onset CAD were included in the study. Although our results are similar to this study, we measured higher SRS and lower SDS. These differences indicate that we observed more fixed defects. The underlying reason for this circumstance is the inclusion of early diagnosed CAD patients together with known cases of long-standing CAD in our study.

White et al. [19] reported that although elevated LDL and triglyceride levels were in correlation with CAD, the association between decreased HDL levels and CAD was suspicious. In accordance with the literature, in CAD+ patients, elevated triglyceride levels and fix defect existence were found to be related in our study. Nevertheless, when all patients and CAD-group were considered, we observed that decreased HDL levels were found to be in association with the presence of fixed defects. According to the results of our study, low HDL is thought to be associated with CAD.

Zakavi et al.[20] have not detected any difference between ischemia and non-ischemia groups in patients without the diagnosis of CAD in terms of total cholesterol, triglyceride, HDL and LDL values. Compatible with this study, our results did not reveal any difference among high triglyceride, LDL levels, and MPS scores. On the other hand, the relationships between high total cholesterol and reversible defect and between decreased HDL level and fixed defect in CAD-group were statistically significant.

In both gender, cardiovascular disease is more common in men at similar ages. This is thought to be due to the protective effect of sex hormones. On the other hand, risk factors that may cause cardiovascular disease are more common in woman[21]. In a study conducted with the European data of WHO, the mortality in females due to CAD was found to be higher[22]. Another study observed more rest perfusion defects in females[23]. In our study, although the perfusion defects were found to be approximately equal in both genders, perfusion defects in males tended to be fixed defect while reversible defects were more common in females.

Our study has several particularly inherited limitations due to its retrospective design. In addition, our patient group is generally composed of low-to-medium-risk groups because of directing high-risk patients directly to the interventional processes without MPS imaging.

According to the protocol of our clinic, stress imaging is performed initially. Then, if there are suspicious defects in the images, the resting imaging is carried out. Otherwise, the second protocol is cancelled. Therefore, low-probability individuals from our patient group were also excluded involuntarily. For this reason, our study remains inadequate to represent all CAD+ or suspected CAD+ patient population.

Conclusion

Herein with this study, EF and gender were determined as independent predictors for SSS while triglyceride levels and gender were for SDS in the same manner. Beyond that, our study demonstrates that fasting blood glucose, lipid profile, gender, and EF values may aid to predict MPS global scores and total perfusion defects.

Ethics

Ethics Committee Approval: The approval of Local Ethical Comittee with a decision number 247, date 30/05/2019 was obtained.

Informed Consent: Informed consent form was obtained from each patient.

Peer-review: Externally and internally peer-reviewed.

Financial Disclosure: The author stated that this study received no financial support.

References

1. Berman DS, Abidov A, Kang X, Hayes SW, Friedman JD, Sciammarella MG, et al. Prognostic validation of a 17-segment score derived from a 20-segment score for myocardial perfusion spect interpretation. Journal of Nuclear Cardiology 2004;11:414-23.
2. Germano G, Kavanagh PB, Slomka PJ, Van Kriekinge SD, Pollard G, Berman DS. Quantitation in gated perfusion SPECT imaging: The Cedars-Sinai approach. Journal of Nuclear Cardiology 2007;14:433-54.
3. Leslie WD, Tully SA, Yogendran MS, Ward LM, Nour KA, Metge CJ. Prognostic value of automated quantification of 99mTc-sestamibi myocardial perfusion imaging. J Nucl Med 2005;46:204-11.
4. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013;34:2949-3003.
5. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation 2003;107:2900-7.

6. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. Circulation 2016;133:e38-360.

7. Srinivasan M, Herrero P, McGill JB, et al. The effects of plasma insulin and glucose on myocardial blood flow in patients with type 1 diabetes mellitus. J Am Coll Cardiol 2005;46:42-8.

8. Mostaza JM, Gomez MV, Gallardo F, et al. Cholesterol reduction improves myocardial perfusion abnormalities in patients with coronary artery disease and average cholesterol levels. J Am Coll Cardiol 2000;35:76-82.

9. Leslie WD, Tully SA, Yogendran MS, Ward LM, Nour KA, Metge CJ. Automated quantification of 99mTc sestamibi myocardial perfusion compared with visual analysis. Nucl Med Commun 2004;25:833-8.

10. Onat A, Büyüköztürk K, Sansoy V, Avcı GŞ, Çam N, Akgün G, et al. Türk Kardiyoloji Derneği Koroner Kalp Hastalığı Korunma ve Tedavi Kılavuzu (Available from: https://www.tkd.org.tr/kilavuz/k11/4e423.htm?wbnum=1604

11. Nasr G, Sliem H. Silent myocardial ischemia in prediabetics in relation to insulin resistance. J Cardiovasc Dis Res 2010;1:116-21.

12. Wu YT, Chien CL, Wang SY, Yang WS, Wu YW. Gender differences in myocardial perfusion defect in asymptomatic postmenopausal women and men with and without diabetes mellitus. J Womens Health (Larchmt) 2013;22:439-44.

13. Oto A. Diabetes and coronary artery disease: Scary duo of the developing world. EJCM 2013;01:45-49.

14. Ghatak A, Padala S, Katten DM, Polk DM, Heller GV. Risk stratification among diabetic patients undergoing stress myocardial perfusion imaging. J Nucl Cardiol 2013;20:529-38.

15. Prior JO, Monbaron D, Koehli M, Calcagni ML, Ruiz J, Bischof Delaloye A. Prevalence of symptomatic and silent stress-induced perfusion defects in diabetic patients with suspected coronary artery disease referred for myocardial perfusion scintigraphy. Eur J Nucl Med Mol Imaging 2005;32:60-9.

16. Romero-Farina G, Candell-Riera J, Aguade-Bruix S, Garcia Dorado D. A novel clinical risk prediction model for myocardial infarction, coronary revascularization, and cardiac death according to clinical, exercise, and gated SPECT variables (VH-RS). Eur Heart J Cardiovasc Imaging 2019;3: pii: jez078.

17. Gimelli A, Rossi G, Landi P, et al. Stress/Rest Myocardial Perfusion Abnormalities by Gated SPECT: Still the Best Predictor of Cardiac Events in Stable Ischemic Heart Disease. J Nucl Med 2009;50:546-53.

18. Schwartz RG, Pearson TA, Kalaria VG, et al. Prospective serial evaluation of myocardial perfusion and lipids during the first six months of pravastatin therapy: coronary artery disease regression single photon emission computed tomography monitoring trial. J Am Coll Cardiol 2003;42:600-10.

19. White J, Swerdlow DI, Preiss D, et al. Association of Lipid Fractions With Risks for Coronary Artery Disease and DiabetesLipid Fractions and Risks of Coronary Artery Disease and DiabetesLipid Fractions and Risks of Coronary Artery Disease and Diabetes. JAMA Cardiol 2016;1:692-9.

20. Zakavi SR, Taherpour M, Moossavi Z, Sadeghi R, Kakhki VD, Rokni H. Clinical value and severity of myocardial perfusion defects in asymptomatic diabetic patients with negative or weakly positive exercise treadmill test. Asia Ocean J Nucl Med Biol 2013;1:14-9.

21. Wakabayashi I. Gender differences in cardiovascular risk factors in patients with coronary artery disease and those with type 2 diabetes. Journal of thoracic disease 2017;9:E503-6.

22. Appelman Y, van Rijn BB, ten Haaf ME, Boersma E, Peters SAE. Sex differences in cardiovascular risk factors and disease prevention. Atherosclerosis. 2015;241:211-8.

23. Byrne C, Kuhl JT, Zacho M, et al. Sex- and age-related differences of myocardial perfusion at rest assessed with multidetector computed tomography. J Cardiovasc Comput Tomogr 2013;7:94-101.

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Effect of Neonatal Hyperbilirubinemia on Ventricular Functions

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Abstract

Objectives: Unconjugated hyperbilirubinemia is a common systemic disease in neonates. Many studies on etiology, risk factors, and treatment have been conducted, and guidelines have been established. Because unconjugated hyperbilirubinemia is a systemic disease, it affects the body, cells, cellular organelles, organs, and systems. Studies have also attempted to clarify the levels, mechanisms, and organs affected by unconjugated bilirubin. We aimed to investigate the effect of high unconjugated bilirubin levels on the left and right ventricular systolic and diastolic functions in newborns by echocardiography and Doppler.

Materials and Methods: This observational retrospective cohort study evaluated neonates with hyperbilirubinemia requiring treatment according to the American Academy of Pediatrics guidelines, who were admitted to our unit between January 2017 and December 2017.

Results: There was no correlation between the serum total bilirubin levels and the echocardiographic measures.

Conclusions: In our study, unconjugated hyperbilirubinemia did not affect the left and right ventricular functions.

Keywords: Neonate, hyperbilirubinemia, cardiac functions

Introduction

Unconjugated hyperbilirubinemia (UCH) is the leading cause of hospitalization and morbidity in neonates(1). Although UCH treatment is well known, the extent of bilirubin damage to the organs and mechanisms is still being investigated. Many studies show that bilirubin exhibits an antioxidant effect at low levels; causes oxidative stress at high levels and damage on organelles, cells, and organs; and affects the autonomic nervous system(2). However, a great number of these

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studies have mainly focused on the neurotoxicity of the oxidative stress induced by high UCH levels; a few studies have investigated the effects of high bilirubin levels on the circulatory system[3,4]. Two *in vitro* studies performed on the effects of UCH on the myocardial tissue show that UCH damages it, and an *in vivo* study determines myocardial functional disorder that can be compensated[5,6]. A number of studies determine that bilirubin levels increase the tone of parasympathetic nervous system and cause heart rate variability[7,8]. To the best of our knowledge, there have been no reports on the high-level UCH effects over the ventricular functions on humans *in vivo*. Our hypothesis is that UCH causes oxidative stress, dysautonomia, myocardial injury, and ventricular dysfunction. In the present study, we aimed to investigate the effect of UCH on ventricular function via transthoracic M-mode and Doppler echocardiographies.

Materials and Methods

An observational retrospective cohort study was conducted to evaluate neonates who were admitted to our unit with hyperbilirubinemia and who required treatment according to the guidelines of the American Academy of Pediatrics between January 2017 and December 2017[1]. Our study group included neonates with a gestational age of 37 to 42 weeks according to the Ballard Score or an ultrasound performed before week 20, appropriate for gestational age (AGA), who were admitted for phototherapy, and who had Doppler echocardiography measurements performed due to heart murmur. Exclusion criteria included the age less than 37 weeks or more than 42 weeks, dehydration, electrolytes, acid-base disorders, polycythemia, anemia, neonatal sepsis, being small for gestational age, intrauterine growth restriction, perinatal asphyxia, congenital anomalies, congenital heart defect, chromosome abnormalities, and lack of data. The control group included 20 healthy infants who had Doppler echocardiography measurements performed due to heart murmur. Total, direct, and indirect bilirubin levels were determined through direct spectrophotometry. Gestational age, birth weight, gender, postnatal age, body weight at the time of enrollment, serum total bilirubin, and Doppler echocardiography measurements were obtained from the patient files.

Echocardiography

Echocardiography was performed by using a Vivid S6 Ultrasound System (GE Healthcare, Milwaukee, WI) according to the American Society of Echocardiography Guidelines[6]. The echocardiographic measurements were performed by a single pediatric cardiologist. Shortening fraction, interventricular septum wall thickness (IVSd), left ventricular end-diastolic (LVED), and left ventricular end-systolic diameters (LVESDs) were obtained by using the M-mode echocardiography by parasternal long axis. Shortening fraction was the difference between the left ventricular end-diastolic and end-systolic diameters; it was calculated by dividing the left ventricular end-diastolic diameter. Left ventricular end-diastolic and end-systolic volumes, and consequently, left ventricular ejection fraction (EF) were measured by the biplane modified Simpson's method.

Tissue Doppler Imaging

A 2-mm pulse-wave (PW) sample volume was placed on the left ventricular septal mitral annulus, the lateral mitral annulus, and the right ventricular lateral tricuspid annulus at the apical four-chamber abutment. The Nyquist limit was adjusted to the range of -20 to 20 cm/s, and a high frame rate (>100 frames s-1) was used. During ventricular systole, positive S, which occurs during early diastolic filling negative E 'and late diastole, left atrial contraction occurs due to the negative wave peak velocities.

Statistical Analysis

Statistical analyses were performed by using IBM SPSS Statistics Base for Windows, version 22.0 (SPSS Inc., Chicago, IL). The student's t-test for independent and paired samples were used to compare continuous variables. Continuous variables are presented as means ± SDs, and categorical variables are given as frequencies with percentages. A p value of less than 0.05 was considered statistically significant.

Results

During the study period, 247 neonates with hyperbilirubinemia requiring treatment were admitted to our unit. Some of those neonates (n=43) were performed Doppler echocardiography and measurements due to heart murmur. Of those admitted patients, 24 of 43 neonates were excluded from the study. Thus, 19 neonates were admitted with hyperbilirubinemia requiring treatment (group 1), 20 healthy infants who had Doppler echocardiography measurements performed due to heart murmur (group 2), were included in the study (Figure 1). Comparisons of the demographic characteristics between the groups are summarized in Table 1. Serum total bilirubin levels, BIND score, and bilirubin/albumin ratio were significantly higher in the study group. M-mode echocardiography measures are shown in Table 2. There were no significant differences in EF, FS, LVEDd, and LVEDs between the two groups. However, the IVSd was found significantly higher in the study group. We found that there were no significant differences in terms of mitral, tricuspid, septal E', A', and S' between groups (Table 3). Furthermore, we could not find any correlation between the serum total bilirubin levels and echocardiographic measures.

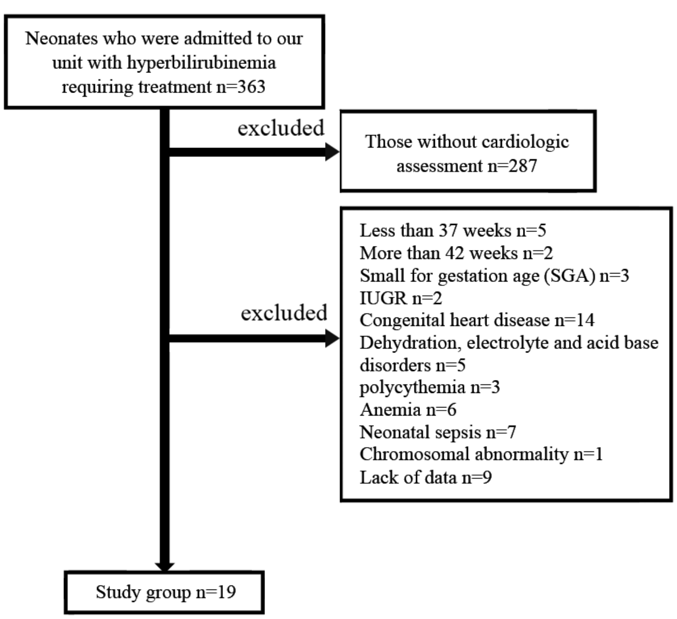

Figure 1. Flowchart of study group

PPROM: Preterm premature rupture of the membranes; IUGR: Intrauterine growth retardation, SGA: Small for gestational age

Discussion

The UCH damage mechanism across organs and systems in neonates is an updated issue that researchers want to investigate. Thus far, studies about the unconjugated bilirubin effects on the central nervous system through the immature blood brain barrier have been conducted[9-11]. However, there are very few studies about the UCH effects on the cardiovascular system. Several studies have been conducted on autonomic control and heart rate variability to demonstrate the relationship between the cardiovascular system and hyperbilirubinemia[5]. There are also two *in vitro* studies

Table 1. Demographical characteristics and laboratory signs of the groups

Parameters	Study group	Control group	p
Gestational age at admission, days (mean ± SD)	4.3±1.1	5.1±1.3	>0.05
Male gender (%)	63.1	55	>0.05
Gestational age, weeks (mean ± SD)	39±1.3	40±1.7	>0.05
Birth weight, g (mean ± SD)	3218±336	3296±341	>0.05
Weight at admission, g (mean ± SD)	3186±304	3212±316	>0.05
Total bilirubin, mg/dl (mean ± SD)	21.7±4.4	4.5±0.9	<0.01
BIND score (mean ± SD)	2.1±0.2	0	<0.01
Bilirubin/Albumin (mean ± SD)	5.3±1.2	1.3±0.2	<0.01

SD: Standard deviation, BIND: Bilirubin-induced neurologic dysfunction

Table 2. Comparison of the echocardiographic measurements between the groups

Parameters	Study group	Control group	p
EF (mean ± SD)	74.5 ± 4.05	78.9 ± 1.3	>0.05
SF (mean ± SD)	44.4 ± 1.2	45.3 ± 1.5	>0.05
LVEDd (mean ± SD)	15.2 ± 0.4	16.2 ± 0.5	>0.05
LVEDs (mean ± SD)	7.7 ± 0.3	8.7 ± 0.3	>0.05
IVSd (mean ± SD)	4.4 ± 0.2	3.7 ± 0.2	>0.05

EF: Ejection fraction, SF: Shortening fraction, LVEDd: Left ventricular end-diastolic diameter, LVEDs: Left ventricular end-systolic diameter, IVSd: Interventricular septum wall thickness (IVSd)

Table 3. Comparison of the Doppler measurements between the groups

Parameters	Study group	Control group	p
Mitral E' (mean ± SD)	5.52 ± 0.46	4.55 ± 0.39	>0.05
Mitral A' (mean ± SD)	6.52 ± 0.32	6.5 ± 0.25	>0.05
Mitral S' (mean ± SD)	4.52 ± 0.24	4.5 ± 0.25	>0.05
Tricuspid E' (mean ± SD)	5.63 ± 0.32	5.1 ± 0.4	>0.05
Tricuspid A' (mean ± SD)	9.05 ± 0.49	9.15 ± 0.59	>0.05
Tricuspid S' (mean ± SD)	5.68 ± 0.32	6.45 ± 0.5	>0.05
Septal E' (mean ± SD)	4.31 ± 0.28	3.8 ± 0.23	>0.05
Septal A' (mean ± SD)	5.57 ± 0.33	6.3 ± 0.44	>0.05
Septal S' (mean± SD)	3.63 ± 0.23	3.85 ± 0.2	>0.05

SD: Standard deviation

investigating the effects of hyperbilirubinemia on myocardial function[12,13]. Even the effect of a systemic disease on the cardiac function is always an updated subject of research, no study has been conducted on the clinical cardiovascular effects of hyperbilirubinemia with echocardiography and tissue Doppler. Basu et al.[3] measured the levels of plasma malondialdehyde (MDA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and total antioxidant status of the neonates. They reported that serum total bilirubin decreased the antioxidant defense effect over 16mg/dL and led to lipid peroxidation with values above 20 mg/dL, resulting in DNA damage of all levels of bilirubin levels. Ostrow et al.[9] have concluded that elevated UCH levels are caused by astrocyte and neuronal apoptosis by mitochondrial and plasma membrane damage. In another study, Paludetto et al.[10] evaluated the behavioral score in neonates with hyperbilirubinemia (mean value=14.3 mg/dL). Brazelton developed a newborn behavioral scoring at the 87th and 104th hours and third week. There was a significant difference in behavior between the two groups at the 87th and 104th hours. They arrived at the end of the 3rd week scoring loss of consciousness. The study of Specq et al.[7] included five preterm lambs with hyperbilirubinemia (150-250 μmol/L) and six healthy preterm lambs. They reported a decrease in breathing rate and increased apnea frequency, and they detected that the inhibition of laryngeal and pulmonary chemoreflexes and bradycardia were more common in the preterm lambs with hyperbilirubinemia. Uhrikova et al.[5] found that UCH caused heart rate variability by disrupting autonomic function. In another study performed with 50 cases with high bilirubin level (20.23±5.53 mg/dL) and 50 healthy newborns, Özdemir et al.[8] found that the mean minimum heart rate, rMSDD, LF, and LF/HF ratio in the study group were significantly lower due to autonomic dysfunction caused by parasympathetic dominance. Bakrania et al.[12] reported that in an *in vitro* study on hyperbilirubinemia, myocardial contractility was reduced, whereas in an *in vivo* study with mice, the ejection fraction and the shortening fraction were the same as in the control group. Gao et al.[13] evaluated CK, CK-MB, Troponin I, and left and right ventricular function via echocardiography in their study of 178 neonates with UCH. They established sufficient evidence that the bilirubin levels caused myocardial damage.

In the present study, we aimed to investigate the effect of bilirubin levels on the right and left ventricular functions through echocardiography. EF and FS could evaluate left ventricular systolic function, the left ventricular systolic functions were the same in both groups, and hyperbilirubinemia did not impair the left ventricular systolic function. The left and right ventricular diastolic functions were evaluated through Doppler echocardiography in both groups considering mitral, tricuspid, septal E', A', S' values. Those measurements were similar in both groups, and hyperbilirubinemia did not impair left and right ventricular diastolic functions.

Conclusions

We report that hyperbilirubinemia does not impair the left and right ventricular function. Therefore, exposure time and severity level of UCH are also as effective as the degree of hyperbilirubinemia in affecting myocardial functions. We conclude that new studies with more severe UCH and larger sample sizes need to be conducted.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.K., A.Ş., Concept: B.K., Design: B.K., Data Collection or Processing: B.K., Analysis or Interpretation: B.K., Literature Search: B.K., Writing: B.K.

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References

1. American Academy of Pediatrics: Management of hyperbilirubinemia in newborn infants 35 or more week of gestation. Pediatrics 2004;114:297-316.
2. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440-63.
3. Basu S, De D, Khanna H, Kumar A. Lipid peroxidation, DNA damage and total antioxidant status in neonatal hyperbilirubinemia. Journal of Perinatology 2014;34:519-23.
4. Kaplan M, Bromiker R, Hammerman C. Severe neonatal hyperbilirubinemia and kernicterus: are these still problems in the third millennium? Neonatology 2011;100:354-62.
5. Uhrikova Z, Zibolen M, Javorka K, Chladekova L,Javorka M. Hyperbilirubinemia and phototherapy in newborns: Effects on cardiac autonomic control. Early Human Development 2015;351-6.
6. Bhavisha B, Eugene F, Toit D, et al. Hyperbilirubinemia modulates myocardial function, aortic ejection, and ischemic stress resistance in the Gunn rat. Am J Physiol Heart Circ Physiol 2014;307:H1142-9.
7. Specq ML, Bourgoin-Heck M, Samson N, Corbin F, Gestreau C, Richer M, et al. Moderate Hyperbilirubinemia Alters Neonatal Cardiorespiratory Control and Induces Inflammation in the Nucleus Tractus Solitarius. Front Physiol 2016;30;7:437.
8. Özdemir R, Olukman Ö, Karadeniz C, et al. Effect of unconjugated hyperbilirubinemia on neonatal autonomic functions: evaluation by heart rate variability, Journal of Fetal Maternal and Neonatal Medicine 2017;31:2763-9.
9. Ostrow JD, Pascolo L, Brites D, Tiribelli C. Molecular basis of bilirubin induced neurotoxicity. Trends Mol Med 2004;10:65-70.
10. Paludetto R, Mansi G, Raimondi F, et al. Moderate hyperbilirubinemia induces a transient alteration of neonatal behavior. Pediatrics 2002;110:e50.
11. Watchko JF. Neonatal indirect hyperbilirubinemia and kernicterus. In: Gleason CA, Devaskar SU (eds). Avery's diseases of the newborn. 9th ed. Philadelphia, Elsevier Saunders; 2012. p. 1123-43.
12. Bakrania B, Toit EF, Ashton KJ, et al. Hyperbilirubinemia modulates myocardial function, aortic ejection, and ischemic stress resistance in the Gunn rat. Am J Physiol Heart Circ Physiol 2014;307:H1142-9.
13. Gao XY, Yang B, Hei MY, et al. Clinical study of myocardial damage induced by neonatal jaundice in normal birth weight term infants. Zhonghua Er Ke Za Zhi 2012;50:343-9.

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Relationships Between Glycemic Control and Platelet Indices, Atherogenic Index of Plasma and Vitamin D in Patients with Type 2 Diabetes

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Abstract

Objectives: Vitamin D deficiency, increased platelet indices and abnormal lipid profile are closely associated with increased vascular complications in type 2 diabetes mellitus (T2DM) patients. We investigated the relationship between glycemic control and platelet indices, vitamin D, atherogenic index of plasma (AIP) and other lipid components in T2DM patients.

Materials and Methods: Diabetic subjects were divided into the groups 1 (good glycemic control, n=59 patients), 2 (moderate glycemic control, n=71 patients), and 3 (poor glycemic control, n=95 patients) according to the HbA1c levels of <7%, 7-9%, and >9%, respectively. We retrospectively analyzed serum lipid profile, platelet count, platelet indices, calcium, phosphorus, vitamin D and HbA1c levels in all patients. The AIP values of the subjects were calculated as follows: AIP=[log triglyceride/high density lipoprotein cholesterol (HDLc)].

Results: In group 1, the mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR), triglyceride and AIP levels were lower, and the HDLc levels were higher than in group 3. Platelet indices, lipid profile, and AIP values of group 2 did not differ from those of group 1 or group 3. There was no difference among the three groups in terms of vitamin D levels. HBA1c levels were positively correlated with the duration of diabetes, triglycerides, AIP, PDW, MPV, and P-LCR, and negatively correlated with HDLc.

Results: Increased platelet indices (MPV, PDW and P-LCR) and AIP values were observed in poor glycemic controlled diabetics. Accordingly, these parameters may be helpful in assessing increased cardiovascular risk in diabetics.

Keywords: Glycemic control, platelet indices, vitamin D, atherogenic index of plasma.

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Introduction

Cardiovascular diseases (CVDs) are a serious complication of type 2 diabetes mellitus (T2DM) and the primary cause of death and disability in diabetics[1]. Abnormal metabolic conditions (such as chronic hyperglycemia, dyslipidemia and insulin resistance) accompanying diabetes may contribute to increased platelet activation and platelet hyperreactivity[2]. Platelet activation, which is known to be associated with cardiovascular risk factors that accelerate atherogenesis[3], can easily be estimated by measuring platelet indices, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet large cell ratio (P-LCR) in automatic complete blood count profiles[4]. MPV, PCT, and PDW levels are reported to be higher in diabetic patients compared to healthy controls[5].

Changes in lipid profiles (increased triglycerides and low-density lipoprotein cholesterol (LDLc) levels and decreased high-density lipoprotein cholesterol (HDLc) levels) are associated with increased cardiovascular event rates in diabetic patients[6]. Increasing evidence indicates that atherogenic index of plasma (AIP), which is defined as log (triglycerides/HDLc), is superior to other lipid parameters in predicting CVD risk[7,8]. It has also been reported that AIP can be used to evaluate the risk of T2DM[9].

The function of vitamin D is not limited to the maintenance of mineral homeostasis and skeletal health but also includes physiological functions in extraskeletal tissues[10]. Substantial evidence suggests that vitamin D affects the mechanisms associated with the pathophysiology of T2DM, including pancreatic beta cell function, insulin action, and secretion[11,12]. Additionally, vitamin D deficiency may increase the risk of cardiovascular disease in diabetics[13,14].

Accumulating evidence has shown a close association between poor glycemic control and the development and progression of diabetes-related complications such as CVD, nephropathy and retinopathy[15,16]. Platelet indices, vitamin D, AIP, and other lipid parameters have been evaluated separately in T2DM patients. Here, we examined the relationship between glycemic control and levels of these parameters in patients with T2DM.

Materials and Methods

This retrospective study was conducted between January 2015 and March 2016 at the Department of Internal Medicine of Mustafa Kemal University Hospital in Hatay Province, Turkey. A total of 225 diabetic subjects were divided into three groups according to their hemoglobin A1c (HbA1c) levels. There were 59 patients with HbA1c <7% (group 1), 71 patients with HbA1c 7-9 % (group 2), and 95 patients with HbA1c >9% (group 3). Group 1, group 2 and group 3 were defined as having good, moderate and poor glycemic control, respectively[17]. Vitamin D (25-hydroxyvitamin D) level of less than 20 ng/mL was considered as hypovitaminosis D[12]. Patients with hematological diseases, active inflammation, infection, liver problems, end stage renal failure and other endocrinology disorders (other than T2DM), pregnancy and malignancy were excluded from the study. None of the patients used anticoagulant medications, vitamin D supplements or lipid-lowering drugs.

Demographic characteristics and laboratory results including lipids, complete blood count, calcium, phosphorus, vitamin D and HbA1c levels of the subjects were obtained from hospital records. Complete blood count analyses were carried out in tubes containing K2 ethylenediamine tetraacetic acid (EDTA) on a Sysmex XN1000 instrument (Sysmex Corp., Kobe Japan) within 2 hours. Serum lipid parameters (total cholesterol, HDLc, LDLc, and triglyceride), calcium and phosphorus levels were run by standard methods on the ARCHITECTc8000 (Abbot, Lake Forest, Illinois, USA). Vitamin D levels were analyzed on an ADVIA Centaur XP Immunoassay System (Siemens, Munich, Germany). HbA1c values of patients were measured by ion-exchange chromatography in a Bio-Rad Variant II system (Bio-Rad, Hercules, CA, USA). Daily quality control was carried out with commercial quality control materials to ensure the precision and accuracy of measurements in our laboratory. The AIP values of patients with T2DM were calculated as follows: AIP=(log triglyceride/HDLc)[18].

Statistical Analysis

Statistical analyses were performed by using SPSS (Version 20, Chicago IL, USA). The normality test of variables was evaluated by using the Kolmogorov-Smirnov test. Differences among the groups in terms of gender distribution were determined using the chi-square test. ANOVA and post-hoc Tukey tests were used to compare normally distributed variables. When the variables were not normally distributed, Kruskal-Wallis test was utilized and pairwise comparisons were performed by using Mann-Whitney U test with Bonferroni correction. Correlations were determined using Spearman and Pearson correlation tests. Significance was accepted at $p<0.05$ ($p<0.0167$ for Mann-Whitney U test with Bonferroni correction).

Results

Demographic and laboratory data of the study groups are provided in Table 1. There were no differences among the three groups according to age, gender distribution, and diabetes duration.

LDLc and total cholesterol levels were similar among the three groups. The triglyceride and AIP values were significantly higher and the HDLc levels were significantly lower in group 3 than in group 1. The triglyceride, HDLc, AIP values of group 2 did not differ from group 1 or group 3.

Platelet count and PCT values were similar in all groups. MPV, PDW, and P-LCR levels were significantly higher in group 3 than in group 1. MPV, PDW and P-LCR levels of group 2 did not differ from those of group 1 or group 3.

The prevalence of hypovitaminosis D was 85.3% (n=192), and that of vitamin D sufficiency was 14.7% (n=33) in patients with T2DM. There were no differences in vitamin D, calcium, and phosphorus levels among groups.

The correlations between HBA1c and other parameters (age, lipid profile, atherogenic index, platelet indices, calcium, phosphorus and vitamin D) are presented in table 2. The levels of HBA1c were positively correlated with the duration of the diabetes, triglycerides, AIP, PDW, MPV and P-LCR, and inversely with HDLc. In addition, vitamin D level was inversely correlated with triglycerides ($r=-0.224$, $p=0.001$) and AIP ($r=-0.202$, $p=0.004$). There was no correlation between platelet indices and AIP and vitamin D levels ($p>0.05$).

Discussion

Accumulating research suggests that dyslipidemia[6], vitamin D deficiency[13,14] and increased platelet indices[19,20] are closely associated with increased cardiovascular events in diabetic populations. Platelet activation is increased in diabetic subjects due to factors such as hyperglycemia, hyperinsulinemia, and atherogenic dyslipidemia[21]. Platelet activation contributes to the increased risk of atherothrombotic events in these patients[2] and can easily be estimated by measuring platelet indices[4].

Many studies have shown that MPV, PCT, PDW, and P-LCR levels are higher in diabetics than in non-diabetic individuals[22-24]. Several authors have also suggested that increased MPV and PDW are associated with the presence of diabetes-related complications in T2DM patients[24-26]. On the other hand, it has been observed that platelet indices tend to decrease in patients with good glycemic control[5,27,28]. Similarly, we determined that MPV, PDW, and P-LCR levels were lower in T2DM patients with good glycemic control compared to the poor glycemic control group, and a positive correlation was observed between HbA1c and these parameters. These results suggest that poor glycemic control contributes to increased platelet activation, thereby increasing cardiovascular events in diabetics.

Patients with T2DM tend to have abnormal lipid profiles that increase cardiovascular event rates[29]. AIP, a newly developed lipid index, is closely associated with the risk of T2DM[9]. Furthermore, high AIP is closely associated with an increased risk of microvascular complications in diabetics[30]. On the other hand, Kocak et al.[31] found that serum cholesterol, LDLc, and TG levels were higher, and HDLc levels were lower, in unregulated diabetic patients (HbA1c ≥7%) compared to regulated diabetics (HbA1c <7%). Another study has emphasized that HbA1c is a good indicator of lipid profile[32]. In the present study, high AIP and triglyceride levels and low HDL levels were observed in the unregulated group (HbA1c >9%) compared to the regulated group (HbA1c <7%). HBA1c levels were positively correlated with triglycerides and AIP, and inversely correlated with HDLc. Collectively, these results showed that in diabetics, lipid

Table 1. Characteristics and laboratory data of study groups

	Group 1 (HbA1c <7%)	Group 2 (HbA1c 7-9%)	Group 3 (HbA1c >9%)	p	Multiple comparisons
Gender (Males; %)	12; 20.3%	21; 29.6%	31; 32.6%	0.251[a]	-
Age (years)	56 (20-75)	59 (23-78)	56 (21-82)	0.342[b]	-
Duration of diabetes (years)	6 (1-30)	7 (1-29)	7 (1-34)	0.081[b]	-
HbA1c (%)	6.3 (5.8-6.9)	7.7 (7-9)	10.5 (9.1-16.5)	**<0.001[b]**	**P_1= <0.001** **P_2= <0.001** **P_3= <0.001**
LDLc (mg/dL)	139.9±39.5	128.7±43.1	130.8±40.6	0.284[c]	-
HDLc (mg/dL)	44.9 (26.8-72.9)	38.6 (24-77.6)	38.8 (22.4-72)	**0.006[b]**	P_1=0.021 **P_2=0.001** P_3=0.544
Cholesterol (mg/dL)	218.5±43.8	204.8±52.1	214.4±46.6	0.267[c]	-
Triglyceride (mg/dL)	132.1 (69.3-358.2)	142.5 (51.5-490.6)	189.8 (59.2-603.8)	**0.005[b]**	P_1=0.333 **P_2=0.002** P_3=0.021
AIP	0.50±0.27	0.58±0.30	0.68±0.29	**0.001[c]**	P_1=0.262 **P_2=0.001** P_3=0.081
Platelet (103/μL)	304±70.8	298.8±83.4	295.9±84.9	0.838[c]	-
PDW (fL)	12.2 (9.6-18)	13.3 (8.3-23)	13.2(8.9-23.4)	**0.002[b]**	P_1=0.032 **P_2= <0.001** P_3=0.271
MPV (fL)	10.4 (9-12.9)	10.8 (8.4-14.2)	10.9 (7.2-14.4)	**0.002[b]**	P_1=0.022 **P_2= <0.001** P_3=0.371
PCT (%)	0.32±0.07	0.32±0.08	0.32±0.08	0.913[c]	-
P-LCR (%)	28.2 (16.9-47.1)	32.1 (15.5-57.7)	33.1 (14-57)	**0.001[b]**	P_1=0.026 **P_2= <0.001** P_3=0.216
Calcium (mg/dL)	9.32±0.55	9.55±0.55	9.41±0.51	0.162[c]	-
Phosphorus (mg/dL)	3.39±0.56	3.53±0.63	3.59±0.58	0.359[c]	-
Vitamin D (ng/mL)	7.5 (4.2-33.9)	10.5 (4.2-52.5)	6.2 (4.2-45.1)	0.177[b]	-

LDLc: Low-density lipoprotein cholesterol, HDLc: High-density lipoprotein cholesterol, AIP: Atherogenic index of plasma, PDW: Platelet distribution width, MPV: Mean platelet volume, PCT: Plateletcrit, P-LCR: Platelet large cell ratio, HbA1c: Hemoglobin A1c
[a]Chi square ($\chi 2$) test, [b]Kruskal-Wallis test, [c]Analysis of variance (ANOVA) test. Post-hoc Tukey test was used for multiple comparisons of AIP, Mann-Whitney U test with Bonferroni correction was used for multiple comparisons of HbA1c, HDLc, triglyceride, PDW, MPV and P-LCR.Significance was accepted at p<0.05 (p<0.0167 for Mann-Whitney test with Bonferroni correction). Bold values indicate statistical significance
P_1 between group 1 and group 2
P_2 between group 1 and group 3
P_3 between group 2 and group 3

Table 2. Correlation between HBA1c levels and other variables in diabetic patients

	HBA1c	
	r	p
Age	0.052	0.437
Duration of diabetes	0.160	**0.016***
LDLc	-0.043	0.537
HDLc	-0.191	**0.006***
Cholesterol	0.038	0.591
Triglyceride	0.274	**<0.001***
AIP	0.290	**<0.001***
Platelet	-0.036	0.596
PDW	0.216	**0.001***
MPV	0.221	**0.001***
PCT	0.011	0.872
P-LCR	0.240	**<0.001***
Calcium	0.017	0.842
Phosphorus	0.167	0.057
Vitamin D	-0.117	0.079

LDLc: Low-density lipoprotein cholesterol, HDLc: High-density lipoprotein cholesterol, AIP: Atherogenic index of plasma, PDW: Platelet distribution width, MPV: Mean platelet volume, PCT: Plateletcrit, P-LCR: Platelet large cell ratio, HbA1c: Hemoglobin A1c
$^*p<0.05$

profile and blood glucose should be controlled to prevent or slow the progression of diabetic complications.

Low vitamin D levels have been shown to be associated with decreased insulin sensitivity and increased risk of developing T2DM[33,34]. For example, Chiu et al.[12] found that vitamin D levels were positively correlated with insulin sensitivity and inversely with glucose. Another study examined the relationship between vitamin D and HBA1c in diabetic patients between November 2016 and June 2017. They found that vitamin D levels were higher in the well-controlled group (HbA1c <8%) than in the poorly controlled group (HbA1c ≥8%)[35]. In contrast, we did not identify differences in vitamin D levels between diabetic groups. This discrepancy may be attributed to the fact that seasonal changes in vitamin D determinations were ignored, and that vitamin D deficiency was present in 85.3% of our diabetic patients. We also found a negative correlation between vitamin D level and triglycerides and AIP. Consistent with our own findings, an observational study showed that vitamin D was inversely related to total cholesterol/HDLc or LDLc/HDLc ratios and triglyceride levels, and that high vitamin D concentrations were related to a favorable lipid panel[36].

The main limitation of this study is that it was a single-center retrospective study. Consequently, we found an association between improved glycemic control in T2DM and decreased MPV, PDW, P-LCR, triglycerides and AIP levels and increased HDLc. Future studies should be conducted to confirm these findings.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Mustafa Kemal University Ethics Committee (Protocol code: 09/05/2016/100).

Informed Consent: Since the study was a retrospective study, informed consent was not obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.M.Ç., Concept: G.Ç., M.M.Ç., Design: G.Ç., M.M.Ç., Data Collection or Processing: G.Ç., M.M.Ç., Analysis or Interpretation: G.Ç., M.M.Ç., Literature Search: G.Ç., Writing: G.Ç., M.M.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Morrish NJ, Wang SL, Stevens LK, Fuller JH, Keen H. Mortality and causes of death in the WHO Multinational Study of Vascular Disease in Diabetes. Diabetologia 2001;44:14-21.
2. Ferroni P, Basili S, Falco A, Davì G. Platelet activation in type 2 diabetes mellitus. J Thromb Haemost 2004;2:1282-91.
3. Davi G, Patrono C. Platelet activation and atherothrombosis. N Engl J Med 2007;357:2482-94.
4. Çakırca G, Çelik MM. Lipid profile and atherogenic indices and their association with platelet indices in familial Mediterranean fever. Turk Kardiyol Dern Ars 2018;46:184-90.

5. Demirtas L, Degirmenci H, Akbas EM, et al. Association of hematological indicies with diabetes, impaired glucose regulation and microvascular complications of diabetes. Int J Clin Exp Med 2015;8:11420-7.

6. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A, del Cañizo-Gómez FJ. Type 2 diabetes and cardiovascular disease: have all risk factors the same strength? World J Diabetes 2014;5:444-70.

7. Cai G, Shi G, Xue S, Lu W. The atherogenic index of plasma is a strong and independent predictor for coronary artery disease in the Chinese Han population. Medicine (Baltimore) 2017; 96:e8058.

8. Zhu L, Lu Z, Zhu L, et al. Lipoprotein ratios are better than conventional lipid parameters in predicting coronary heart disease in Chinese Han people. Kardiol Pol 2015;73:931-8.

9. Zhu XW, Deng FY, Lei SF. Meta-analysis of atherogenic index of plasma and other lipid parameters in relation to risk of type 2 diabetes mellitus. Prim Care Diabetes 2015;9:60-7.

10. Reid IR, Bolland MJ. Skeletal and nonskeletal effects of vitamin D: is vitamin D a tonic for bone and other tissues? Osteoporos Int 2014;25:2347-57.

11. Zeitz U, Weber K, Soegiarto DW, Wolf E, Balling R, Erben RG. Impaired insulin secretory capacity in mice lacking a functional vitamin D receptor. FASEB J 2003;17:509-11.

12. Chiu KC, Chu A, Go VLW, Saad MF. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. Am J Clin Nutr 2004;79:820-5.

13. Cigolini M, Iagulli MP, Miconi V, Galiotto M, Lombardi S, Targher G. Serum 25-hydroxyvitamin D3 concentrations and prevalence of cardiovascular disease among type 2 diabetic patients. Diabetes Care 2006;29:722-4.

14. Targher G, Bertolini L, Padovani R, et al. Serum 25-hydroxyvitamin D3 concentrations and carotid artery intima-media thickness among type 2 diabetic patients. Clin Endocrinol (Oxf) 2006;65:593-7.

15. Ceriello A, Ihnat MA, Thorpe JE. Clinical review 2: The "metabolic memory": is more than just tight glucose control necessary to prevent diabetic complications? J Clin Endocrinol Metab 2009;94:410-5.

16. Fasil A, Biadgo B, Abebe M. Glycemic control and diabetes complications among diabetes mellitus patients attending at University of Gondar Hospital, Northwest Ethiopia. Diabetes, Metab Syndr Obes 2019;12:75-83.

17. Chiang CY, Lee JJ, Chien ST, et al. Glycemic control and radiographic manifestations of tuberculosis in diabetic patients. PLoS One 2014;9:e93397.

18. Dobiásová M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). Clin Biochem 2001;34:583-8.

19. Sahin DY, Gür M, Elbasan Z, et al. Mean platelet volume and extent and complexity of coronary artery disease in diabetic and nondiabetic patients with ST elevation myocardial ınfarction. Angiology 2013;64:505-11.

20. Tavil Y, Sen N, Yazici H, et al. Coronary heart disease is associated with mean platelet volume in type 2 diabetic patients. Platelets 2010;21:368-72.

21. Ferreiro JL, Gómez-Hospital JA, Angiolillo DJ. Platelet abnormalities in diabetes mellitus. Diab Vasc Dis Res 2010;7:251-9.

22. Shilpi K, Potekar RM. A study of platelet indices in type 2 diabetes mellitus patients. Indian J Hematol Blood Transfus 2018;34:115-20.

23. Alhadas K, Santos SN, Freitas MMS, Viana SMSA, Ribeiro LC, Costa MB. Are platelet indices useful in the evaluation of type 2 diabetic patients? J Bras Patol Med Lab 2016;52:96-102.

24. Jindal S, Gupta S, Gupta R, et al. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. Hematology 2011;16:86-9.

25. Xiao W, Huang Y, Dong J, Zhang X, Hu J. Relationship between platelet volume indices with macrovascular and peripheral neuropathy complications in type 2 diabetic patients. J Diabetes 2014;6:298-303.

26. Papanas N, Symeonidis G, Maltezos E, et al. Mean platelet volume in patients with type 2 diabetes mellitus. Platelets 2004;15:5-9.

27. Ulutas KT, Dokuyucu R, Sefil F, et al. Evaluation of mean platelet volume in patients with type 2 diabetes mellitus and blood glucose regulation: a marker for atherosclerosis? Int J Clin Exp Med 2014;7:955-61.

28. Demirtunc R, Duman D, Basar M, Bilgi M, Teomete M, Garip T. The relationship between glycemic control and platelet activity in type 2 diabetes mellitus. J Diabetes Complications 2009;23:89-94.

29. Nayak BS, Butcher DM, Bujhawan S, et al. Association of low serum creatine, abnormal lipid profile, gender, age and ethnicity with type 2 diabetes mellitus in Trinidad and Tobago. Diabetes Res Clin Pract 2011;91:342-7.

30. Zoppini G, Negri C, Stoico V, Casati S, Pichiri I, Bonora E. Triglyceride-high density lipoprotein cholesterol is associated with microvascular complications in type 2 diabetes mellitus. Metabolism 2012;61:22-9.

31. Kocak MZ, Aktas G, Erkus E, Sincer I, Atak B, Duman T. Serum uric acid to HDL-cholesterol ratio is a strong predictor of metabolic syndrome in type 2 diabetes mellitus. Rev Assoc Med Bras 2019;65:9-15.

32. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. Clin Exp Med 2007;7:24-9.

33. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. Diabetes Care 2005;28:1228-30.

34. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes Care 2004;27:2813-8.

35. Erkus E, Aktas G, Kocak MZ, Duman TT, Atak BM, Savli H. Diabetic regulation of subjects with type 2 diabetes mellitus is associated with serum vitamin D levels. Rev Assoc Med Bras 2019;65:51-5.

36. Jorde R, Grimnes G. Vitamin D and metabolic health with special reference to the effect of vitamin D on serum lipids. Prog Lipid Res 2011;50:303-12.

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Tricuspid Valve Ring Annuloplasty in a Patient with 36-year *in-situ* Functioning Bjork-Shiley Valve in Mitral Position

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Abstract

The Bjork-Shiley valve (BSV) was one of the first tilting disc valve prostheses that were used. We report a patient with a still functioning BS mitral valve prosthesis implanted and required a redo surgery for tricuspid valve regurgitation.

Keywords: Bjork-Shiley valve, tricuspid regurgitation, ring annuloplasty

Introduction

The Bjork-Shiley (BS) mechanical valve (ShileyCorp, Irvine, CA) was the first tilting disc valve used for the management of valvular heart disease[1]. It was one of the most implanted mechanical valves between 1970s and 1980s; however, the valve's production was stopped due to increased rate of fracture and disc escape that resulted in high patient mortality. We report a patient with a BS mitral valve prosthesis implanted in 1981 and still functioning.

Case Report

A 56-year-old female patient with the symptoms of leg swelling and dyspnea resulted from right ventricular failure was admitted to our clinic. She had undergone a mitral valve replacement with a BS tilting disc valve 36 years ago (Figure 1). Her echocardiogram revealed

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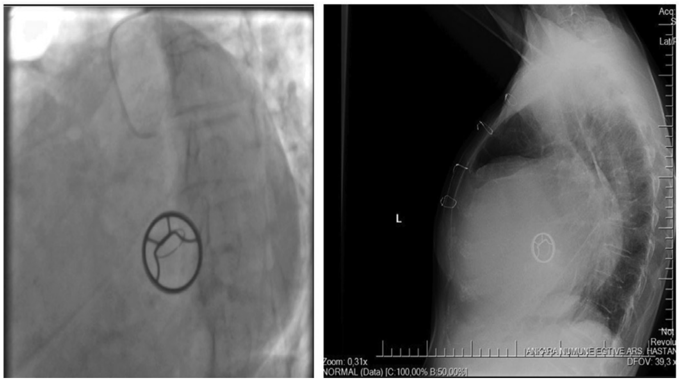

Figure 1. A. Preoperative coronary angiogram view showing Bjork-Shiley tilting disk valve in mitral position, B. Preoperative lateral chest X-ray view showing Bjork-Shiley tilting disk valve in mitral position

a well-seated, normally functioning prosthetic mitral valve with a mean pressure gradient of 5 mmHg. The left atrium was enlarged (8 cm) and the left ventricle remained normal in size. Left ventricular systolic function was normal with an estimated ejection fraction of 65%. The size of the right atrium was 12x10 cm, the diameter of the inferior vena cava was 4.1 cm. She had a severe tricuspid valve (TV) regurgitation and moderate pulmonary hypertension (systolic pulmonary artery pressure=50 mmHg). Tricuspid regurgitant velocity (TRV) was 3.3 m/s and tricuspid annular plane systolic excursion (TAPSE) was 13mm. We planned to perform only TV repair and not to touch the functioning BS valve.

After obtaining informed consent from the patient for both the surgery and the use of her medical records, resternotomy was carried out using cardiopulmonary bypass under the right femoral artery and vein cannulation. We decided to perform TV repair without an aortic cross-clamp, so we did not arrest the heart. We explored the TV through the right atriotomy while the heart was beating and implanted a 3D tricuspid annuloplasty ring (Size=32 mm, CONTOUR 3D®, Medtronic, USA).

Postoperative recovery was uneventful. The postoperative control echocardiography showed normal functioning BS valve in mitral position and no TV regurgitation was observed. She was discharged on the 5th postoperative day and she is doing well for 18 months after the procedure.

Discussion

The BS valve was the first tilting disc mechanical valve implanted for heart valve replacement[1]. It was a low-profile mechanical valve with a Delrin disc. As this initial Delrin disc resulted in many structural complications such as wear or fracture, it was replaced by a pyrolytic carbon[2,3]. However, these structural changes of the BS valve could not prevent the valve from strut fractures and in the end, BSV was recalled from the market. In the literature, there are many case series and reports that show structural deformities of the BSV[4-6]. There are also case reports about BSV, which suggest that these valves are still functioning for 25- 42 years[7,8].

Prophylactic replacement of these valves which were prone to fracture was a concern especially in the early years of implantation of BSV and this peak of replacement was mainly due to infective endocarditis[9]. The other peaks of replacement were mainly after the identification and publication of risk factors for outlet strut fracture in 1992[10]. However, there have been debates on the necessity of these replacements. Guidelines for BS valve replacement were introduced to prevent unnecessary reoperations and these had a positive effect on treatment decisions[10].

Conclusion

The implanted valve in our patient has been functioning well for 36 years. The patient underwent a TV repair for TV regurgitation. BSV that was implanted in our patient had no structural abnormalities and it was functioning with a low-pressure gradient (5 mmHg). We decided to keep this normal functioning and non-destructed valve in place and not to perform a left atriotomy. We performed ring annuloplasty through right atriotomy and the postoperative course was uneventful. Since we did not touch the working BSV, we could perform beating heart TV repair and we think that these precautions resulted in an uncomplex operation and uneventful perioperative period.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions

Surgical and Medical Practices: A.T.K., K.Ö., S.G., O.E.G., Concept: A.T.K., N.B.T., A.B.B., Design: A.T.K., N.B.T, A.B.B., Data Collection or Processing: A.T.K., K.Ö., S.G., O.E.G., S.G., Analysis or Interpretation: A.T.K., N.B.T., O.E.G., Literature Search: A.T.K., Writing: A.T.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Björk VO. A new tilting disc valve prosthesis. Scand J Thorac Cardiovasc Surg 1969;3:1-10.
2. Björk VO. Disc wear in the Björk-Shiley tilting disc valve. Experiment and clinical observation. Scand J Thorac Cardiovasc Surg 1971;5:87-91.
3. Björk VO. The pyrolytic carbon occluder for the Björk-Shiley disc valve prosthesis. Scand J Thorac Cardiovasc Surg 1972;6:109-13.
4. Cane ME, McGrath LB. Elective reoperation for a strut fracture in a Björk-Shiley convexo-concave mitral valve. Ann Thorac Surg 1994;58:1184-5.
5. Scalia D, GiacominA, Da Col U, et al. Successful treatment of a patient after sudden loss of the disc in a Björk-Shiley convexo-concave mitral prosthesis. Thorac Cardiovasc Surg 1987;35:318-20.
6. Uchino G, Yoshida H, Sakoda N, et al. Outlet strut fracture and leaflet escape of Bjork-Shiley convexo-concave valve. Gen Thorac Cardiovasc Surg 2017;65:358-60.
7. Gunn JM, Malmberg M, Vähäsilta T, et al. Thirty-year results after implantation of the Björk-Shiley Convexo-Concave Heart valve prosthesis. Ann Thorac Surg 2014;97:552-6.
8. Shaikh A, Jamil Tajik A. Excellence and Durability: A Normally Functioning Björk-Shiley Flat-Disc Prosthesis 42 Years Post Implantation. J Heart Valve Dis 2016;25:237-9.
9. Mansur AJ, Dal Bó CM, Fukushima JT, et al. Relapses, recurrences, valve replacements, and mortality during the long-term follow-up after infective endocarditis. AmHeart J 2001;141:78-86.
10. van Gorp MJ, Steyerberg EW, van der Graaf Y. Decision guidelines for prophylactic replacement of Björk-Shiley convexo-concave heartvalves: impact on clinical practice. Circulation 2004;109:2092-6.

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A Rare Complication after TAVI: Acute Left Main Coronary Artery Occlusion and Successful Percutaneous Treatment

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Abstract

Aortic valve stenosis is common in the elderly. Nowadays surgical aortic valve replacement has still been the gold standard of management, but many patients have been excluded from surgery given that they are very old, frail, or have comorbidities that increase operative risks. In the last decade, transcatheter aortic valve implantation (TAVI) has emerged as a new treatment option for these patients. Despite its being less invasive than surgery, TAVI has rare but fatal complications like vascular injuries. Vascular injuries are the most common complications after TAVI, and they range from dissection to perforation and acute thrombotic occlusion. We report a case of left main coronary artery occlusion following TAVI that caused cardiac arrest and was managed successfully with emergency percutaneous coronary intervention.

Keywords: Transcatheter aortic valve implantation (TAVI), percutaneous coronary intervention, left main occlusion

Introduction

Transcatheter aortic valve implantation (TAVI) is an alternative treatment to surgical aortic replacement in patients who have severe aortic stenosis and high surgical risk[1]. Since its first description in 2002, it has been performed successfully in worldwide[2]. But despite its being less invasive than surgery, TAVI has rare but fatal complications like coronary obstruction. We report here a case of left main coronary artery (LMCA)

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occlusion following TAVI that caused cardiac arrest and was managed successfully with emergency percutaneous coronary intervention (PCI).

Case Report

An 83-year-old male patient presented to our clinic with decompensated heart failure. He had hypertension, diabetes, and chronic obstructive pulmonary disease. On the physical examination, we found common rales in both lungs. Echocardiogram showed severe aortic stenosis (Pg Max/Mean=110/60 mmHg) and normal LV ejection fraction, 2-3. degree mitral regurgitation, 3. degree aortic regurgitation, and 2. degree tricuspid regurgitation. His systolic pulmonary artery pressure was 55 mmHg. After the stabilization of the patient, the risk scores were calculated for aortic surgery (Log. Euroscore was 21%, Euroscore 2 was 14 %, STS score was 8,7 %) and the patient was accepted to have high surgical risk for surgery in our cardiology, cardiovascular surgery, and cardiac anesthesia joint committee. So, we decided to perform TAVI. The super-stiff wire was inserted into the left ventricle through the left Amplatz-2 catheter via left femoral artery. The delivery system was advanced and predilatation was performed by creating hypotension at the level of the aortic valve under high-speed pacemaker (Figure 1A). Then, 29 mm Edwards Sapien XT aortic valve level was adjusted and the valve was implanted using balloon under high-speed pacemaker (Figure 1B, 1C). Valve placement was performed without any complications. No complication was detected in the patient's aortography and the procedure was ended. While the femoral closure was going on, the patient's hemodynamic impaired and then the patient had cardiac arrest and was immediately intubated. Echocardiography showed no pericardial effusion. At fluoroscopy, bioprosthetic valve was in place. Coronary angiography was performed from the contralateral groin. There was no flow from the proximal left main coronary artery (Figure 1D). Then, under the CPR, a 0,014-inch guidewire was advanced into LAD and multiple balloon angioplasty was performed with a 2.5x15 and 3.0x20 mm balloon (Figure 2A, 2B). A 3.5x25 mm Commander BMS was implanted from LMCA to LAD and TIMI 2 flow was provided both in LAD and CFX artery. Then, the patient's rhythm was achieved. (Figure 2C, 2D). The patient was taken to the intensive care unit. He was arrested again after 5 hours and the rhythm could not be achieved despite the CPR for 45 minutes and the patient was exitus.

Discussion

TAVI includes the insertion of a prosthetic valve into the stenotic aortic valve through a vascular access without the need for open heart surgery. Despite its widespread use and increasing experience of surgeons, TAVI has life-threatening complications especially vascular injuries. Complication rates differ with the experience of surgeon, the size of the device, the site of catheter access, as well as the use of pre-procedural screening. The coronary obstruction was first reported in 2006 by Webbs. The frequency of this complication ranges from 0% to 4 % but the mean frequency has been reported as 1% in large studies[3-8]. Clinical manifestation of this

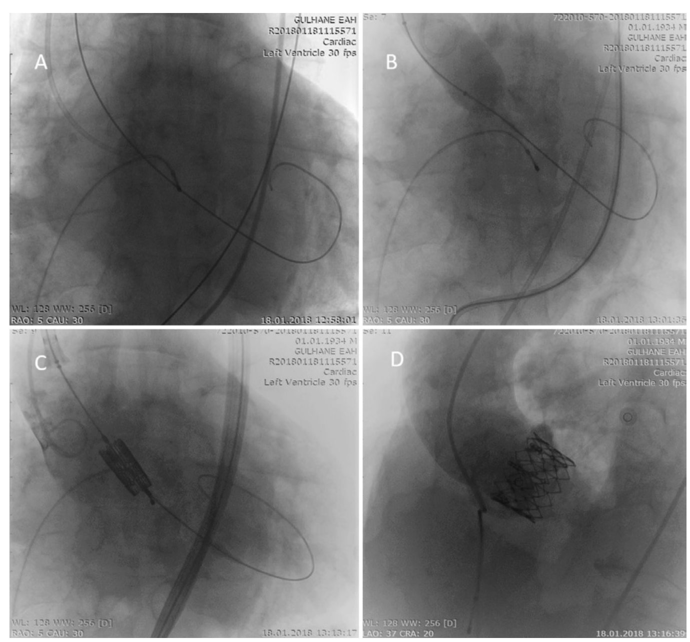

Figure 1. A. Predilatation was performed by creating hypotension under high-speed pacemaker. **B.** 29 mm Edwards Sapien XT aortic valve level was adjusted. **C.** 29 mm Edwards Sapien XT aortic valve was implanted using a balloon under a high-speed pacemaker. **D.** Coronary angiography showed total occlusion of the left main coronary artery

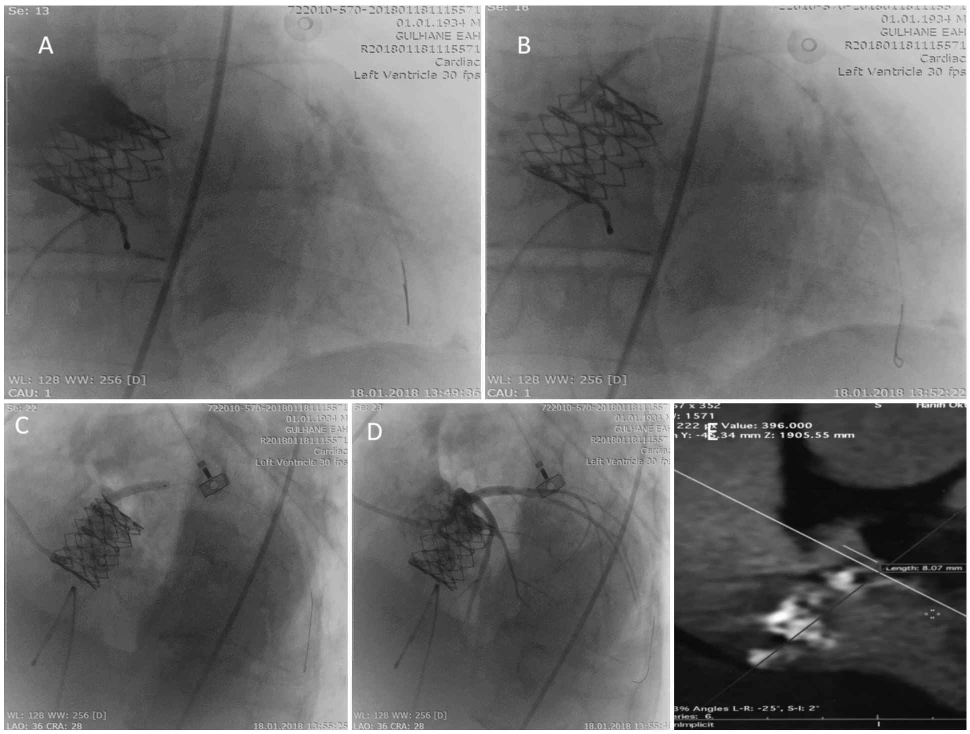

Figure 2. **A.** PTCA was performed with a 2.5x15 and 3.0x20 mm balloons. **B.** 3.5x25 mm Commander BMS was implanted from LMCA to LAD. **C.** After stent, TIMI 2 flow was provided both LAD and CFX. **D.** The distance between left coronary ostium and aortic annulus was 8.02 mm

situation usually includes persistent hypotension, ST segment changes (elevation or depression), ventricular arrhythmias and sudden cardiac arrest immediately after valve implantation.[6] The most known risk factors of this complication are shorter (<10 mm) distance between the left coronary ostium and aortic annulus, narrow aortic annulus, the presence of bulky calcium nodules on aortic leaflets, and use of balloon-expandable valve[(6,9)]. Coronary ostium height cut off level of 10 mm or shorter increases the risk of coronary obstruction[(10)]. Kapadia et al.[(11)] recommended that a 0.014 mm guidewire can be advanced into LAD through a guiding catheter during valve deployment so that we can quickly access and if necessary dilate the left main trunk. In cases of severe hypotension, ST segment changes (elevation or depression), ventricular arrhythmias and sudden cardiac arrest, LMCA occlusion is the major complication apart from rupture. In such a situation, emergency angiography must be performed and coronary obstruction must immediately be treated with angioplasty and stenting. In failed percutaneous interventions, even coronary artery bypass (CABG) can also be performed and it may require Tandem Heart support [(9,11,12)] Normally in our institution, we routinely take CT angiography before the TAVI procedure. In our case the distance between left coronary ostium and aortic annulus was 8.02 mm (Figure 2E). In our patient, we believe that shorter left coronary ostium height and bulky calcific nodule on aortic leaflet caused left main coronary occlusion. In a retrograde review, we did not advance a guidewire into LAD but we treated the patient successfully with stenting and after stenting the rhythm was achieved.

Conclusion

As a result, in situations following TAVI, such as severe hypotension, ST segment changes (elevation or depression), ventricular arrhythmias, and sudden cardiac, arrest emergency coronary angiography must be performed from the contralateral groin and LMCA occlusion must be treated with emergency angioplasty and stenting. In the TAVI procedure, a detailed preoperative evaluation is as important as the procedure.

Ethics

Informed Consent: The study was conducted in accordance with the international agreements and the Declaration of Helsinki, and informed consent for the study was taken from the patient's son.

Authorship Contributions

Surgical and Medical Practices: Ö.F.K., A.İ., Concept: M.D., Design: M.D., Data Collection or Processing: Ö.F.K., A.İ., Analysis or Interpretation: Ö.F.K., A.İ., Literature Search: Ö.F.K., M.D.,Writing: Ö.F.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017;38:2739-91.
2. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006-8.
3. Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. Journal of the American College of Cardiology 2007;50:69-76.
4. Himbert D, Descoutures F, Al-Attar N, et al. Results of transfemoral or transapical aortic valve implantation following a uniform assessment in high-risk patients with aortic stenosis. Journal of the American College of Cardiology 2009;54:303-11.
5. Jilaihawi H, Chakravarty T, Weiss RE, et al. Meta-analysis of complications in aortic valve replacement: comparison of Medtronic-Corevalve, Edwards-Sapien and surgical aortic valve replacement in 8,536 patients. Catheterization and cardiovascular interventions: official journal of the Society for Cardiac Angiography & Interventions 2012;80:128-38.
6. Ribeiro HB, Nombela-Franco L, Urena M, et al. Coronary obstruction following transcatheter aortic valve implantation: a systematic review. JACC Cardiovasc Interv 2013; 6:452-61.
7. Stabile E, Sorropago G, Cioppa A, et al. Acute left main obstructions following TAVI. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 2010;6:100-5.
8. Webb JG, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. Circulation 2006;113:842-50.
9. Ergene O, Emren V, Duygu H, et al. [A case of occurring hemodynamic deterioration and ST-segment elevation during transcatheter aortic valve implantation]. Turk Kardiyoloji Dernegi arsivi: Turk Kardiyoloji Derneginin yayin organidir 2014;42:556-9.
10. Holmes DR Jr, Mack MJ, Kaul S, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. Journal of the American College of Cardiology 2012;59:1200-54.
11. Kapadia SR, Svensson L, Tuzcu EM. Successful percutaneous management of left main trunk occlusion during percutaneous aortic valve replacement. Catheterization and cardiovascular interventions: official journal of the Society for Cardiac Angiography & Interventions 2009;73:966-72.
12. Dagdelen S, Karabulut H, Alhan C. Acute left main coronary artery occlusion following TAVI and emergency solution. Anadolu kardiyoloji dergisi: AKD = the Anatolian journal of cardiology 2011;11:747-8.

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These mistakes have made by author inadvertently. The errors correction in the article has been demonstrated in the following list:

Error

[1]Kemalpaşa State Hospital, Clinic of Cardiology, İzmir, Turkey

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Correction

[1]Kemalpaşa State Hospital, Clinic of Cardiology, İzmir, Turkey

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