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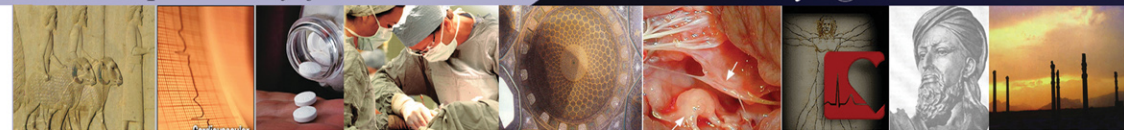
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Risk factors of short-term stroke recurrence in patients with minor ischemic cerebrovascular events

Kavian Ghandehari⁽¹⁾, Mohammad Reza Khajedaluei⁽²⁾, Zahra Yazdankhah⁽³⁾,
Kosar Ghandehari⁽⁴⁾

Original Article

Abstract

BACKGROUND: Assessing the risk of recurrent ischemic events in patients with transient ischemic attack (TIA) and minor ischemic stroke (MIS) is of a great importance in clinical practice.

METHODS: Consecutive patients with TIA or MIS who were visited in Ghaem Hospital, (Mashhad, Iran) were enrolled in a prospective cohort study during 2010 to 2011. Diagnosis of TIA or MIS was accomplished by a stroke neurologist. Only those who presented within 24 hours from the onset of symptoms were recruited. MIS was considered as an ischemic stroke with National Institutes of Health Stroke Scale (NIHSS) < 4. The endpoint of the study was a new ischemic cerebrovascular event or vascular death in 90 days and additionally in 3 days. The decision to admit and type of treatment in each case was left to the discretion of the stroke neurologist. The association between 20 potential factors with recurrent ischemic events in 3 and 90 days was investigated using univariate and multivariate analysis (MVA).

RESULTS: 393 TIA patients (238 males and 155 females) and 118 MIS patients (77 males and 41 females) were enrolled in the study. Stroke occurred in 117 (23.2%) patients, TIA in 99 (19.6%), and there was 11 (2.2%) vascular deaths within 3 months in the total 511 patients with minor ischemic events. Crescendo TIAs and multiple TIAs were associated with greater risk of stroke in 3 days in a univariate analysis (OR = 5.12, P < 0.001) and (OR = 3.98, P = 0.003), respectively. Patients with index stroke had 11.5% lower risk of recurrent stroke in 3 days than patients with index TIA in multivariate analysis (OR = 0.115, P = 0.039). Diabetes was independently associated with 3 months stroke recurrence in the patients with minor ischemic events (OR = 2.65, P = 0.039).

CONCLUSION: Multiple and crescendo TIAs are the main predictors of stroke recurrence, derived from the univariate analysis of the patients with minor ischemic events.

Keywords: Transient Ischemic Attacks, Infarction, Brain, Recurrence, Risk

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Introduction

The approach for management of patients with transient ischemic attack (TIA) or minor ischemic stroke (MIS) has been remained variable and controversial.¹ Reliable and easily obtainable information on each patient risk profile should be promptly available in the emergency setting to guide the management.² A large number of TIA and MIS patients do not go on to experience an early stroke. These patients do not need to be exposed to potentially risky therapies from which they will drive

no benefit, nor do they need to use high-intensity resources. The clinical imperative is to sort out those patients who need immediate attention and those who do not. Because there is no single prognostic factor for TIA patients differentiating who are going to suffer an event or not, it is very difficult to achieve perfect discrimination.³ TIA heralds a relatively high risk of stroke between 10% and 20% in the ensuing 90 days and half of the risk of early stroke occurs in the first 2 days after TIA.^{4,5} In managing patients with TIA or MIS, it would be

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useful to know a given patient risk for having a stroke in the near future.⁶ Identification of predictive factors in short-term recurrence of ischemic cerebrovascular events in TIA and MIS patients constitutes the objectives of the present study.

Materials and Methods

Patients with consecutive TIA or MIS were prospectively evaluated in Ghaem Hospital and Stroke Clinic (Mashhad, Iran) during 2010-2011. This prospective cohort study included patients with initial TIA or MIS with or without (as control) subsequent ischemic cerebrovascular events. Diagnosis of TIA or MIS was done by a stroke neurologist. Only those who presented within 24 hours from the onset of symptoms were enrolled.² Whether the initial ischemic symptoms lasted less than or more than 24 hours, categorized the patients as TIA or MIS, respectively. Patients had to access the hospital or stroke clinic within 24 hours of post event to enhance precise recall of the type and duration of symptoms and to guarantee inclusion of very short-term strokes.² Patients were enrolled in this study if they had a Pre-morbid Modified Rankin Scale ≤ 1 .⁵ Ischemic stroke and TIA was defined as a sudden focal neurologic deficit of presumed arterial origin lasting ≥ 24 hours and < 24 hours, respectively with or without corresponding ischemic lesion on brain imaging.⁸ MIS was considered as an ischemic stroke with National Institutes of Health Stroke Scale (NIHSS) < 4 .⁵ Exclusive criteria were clinical evaluation over 24 hours from the end of the transient event and a final diagnosis of non-ischemic causes of symptoms such as migraine, seizure and anxiety.⁷ A known cognitive impairment and a significant comorbidity limiting participation in the study also was considered as exclusive criteria.¹ The patients with disabling stroke, defined as NIHSS ≥ 4 in 1 day after event to allow for a more reliable assessment of recurrent events were excluded from the study.⁸ The endpoint of the study was a new ischemic cerebrovascular event or vascular death in 90 days and additionally in 3 days. Recurrent TIA, stroke and vascular death as well as the hospital admission and ongoing medication were recorded.⁷ Recurrent stroke was considered as the exacerbation by at least 4 points in the initial NIHSS punctuation or clearly defined new symptoms of > 24 hours duration that suggested a new ischemic event.^{9,10} A recurrent TIA was defined as a new neurologic symptom of < 24 hours duration that was caused by focal ischemia in the brain or retina.^{1,11} Follow up data were obtained

from direct patient visit in 3 and 90 days or by centralized telephone interview if patients failed to attend the visit.⁹ Follow up was continued until death or 3 months from the date of the index event.¹ All recurrent TIA and stroke were assessed and investigated by a stroke neurologist.⁷ Vascular death was defined by acute coronary syndrome or cerebrovascular syndrome certified as the cause of death or contributing directly to death.¹ In patients who had multiple recurrent events, the endpoint was classified as the first recurrence after the index ischemic event.¹⁰ All patients underwent blood test, ECG, head scan and duplex ultrasound of neck arterial trunks.^{6,12} The decision to admit and treatment in each case was left to the discretion of the stroke neurologist. A strict control of vascular risk factors after discharge in all cases was recommended. Antiplatelet therapy was recommended in acute phase of all the patients with exception of those with cardioembolic strokes, patients already pretreated with antiplatelet, patients with crescendo TIA or progressive stroke after antiplatelet treatment in whom anticoagulation was initiated.⁹

A detailed history was taken from each TIA or MIS patient with a standardized questionnaire which included following variables. As far as possible, variables were defined and categorized in the same way as had been predictive in previous studies.¹⁻¹³ Age was dichotomized at 60 years.¹³ Clinical features were categorized as motor weakness (focal and unilateral weakness of one or more of face, arm, hand or leg) versus speech disturbances (defined as either dysarthria or dysphasia stroke or both).¹³ Limb weakness required a clear description of loss of power as opposed to more vague terms such as clumsiness or heaviness.¹³ Isolated sensory or visual symptoms were also recorded in the patients.¹⁴ Duration of symptoms was categorized as less than 10 minutes, 10-59 minutes, and 60 minutes or longer.¹³ Hypertension was defined as using antihypertensive medication or patients with two blood pressure values (at least 1 week interval) of $> 140/90$ mm/Hg.^{6,15} Administration of antidiabetic medication or a fasting blood glucose > 6.4 mmol/L or > 126 mg/dL were definitions of diabetes mellitus.^{2,9,15} Hyperlipidemia was defined as use of lipid lowering medication, serum cholesterol concentration > 5.2 mmol/L or > 220 mg/dL, LDL cholesterol > 130 mg/dL, or serum triglyceride concentration > 150 mg/dL.^{9,15} Current smoking habits was also recorded.⁹ Patients who smoked more than 5 cigarettes per day in recent year were defined as smoker.^{15,16} Stroke was analyzed for the non-TIA

index event (the distinction between MIS and TIA was determined by the presence of symptoms lasting > 24 hours). Duplex ultrasound served for detection of $\geq 70\%$ carotid stenosis corresponding to manifestations.^{17,18} Acute stroke signs in brain CT performed within 24 hours post event, previous history of stroke or TIA, and prior TIA in previous 7 days named as multiple TIA.^{9,19} Cardiac risk factors included atrial fibrillation (prior documented history or evidence in the baseline ECG);^{2,19} coronary artery disease (evidence in the baseline ECG or documented prior history of angina pectoris or myocardial infarction);^{9,19} other high risk cardioembolic sources (defined if long-term anticoagulation was indicated based on findings in previous medical record, ECG or echocardiography).^{19,20} Crescendo TIAs was defined as two or more TIAs within the past week with increasing in duration and in severity of deficit.^{21,22} The 3 days and 90 days risk of TIA or stroke was determined in relation to each variable¹³. The successful follow up percentage was 92% and patients without complete follow-up were not analyzed and omitted from the results. Data on demographics and above variables were recorded in a standardized questionnaire and entered in SPSS for Windows 16.0 (SPSS Inc., Chicago, IL, USA). The primary analysis estimated the proportion of patients with endpoints for each category of variables. Differences of all the variables in the univariate analysis were evaluated by chi-square and Fisher's exact tests. Multivariable odds ratios (OR) with 95% CI were calculated in the secondary analysis of recurrence predictors using a multiple logistic backward regression model. The research was approved by the Ethics Committee of Ghaem Hospital, and an inform consent was obtained from the patients. There was no delay in any of the therapeutic interventions in order to continue the present study.⁹

Results

A total of 511 patients (315 and 196 males and females, respectively) meeting the eligibility criteria were recruited and completed the follow-up study during 2010 to 2011. Three hundred and ninety three TIA patients (238 and 155 males and females, respectively) and 118 MIS patients (77 and 41 males and females, respectively) were enrolled in the study. 72.4% of the patients (370 out of 511) were admitted in the hospital and the others were recruited from the stroke clinic. The mean age of all the patients was 68.5 ± 4.7 years and 63.2% of the patients were ≥ 60 years of age. The elapsed time

from symptom onset to evaluate the index event was less than 24 hours in all the cases (14.6 ± 2.2 hours). The mean age of TIA and MIS patients was 68.4 years and 66.2 years, respectively. 117 strokes (23.2%), 99 TIA (19.6%), and 11 vascular deaths (2.2%) occurred within 3 months of post event in total of 511 patients with minor ischemic events. The estimated risk of recurrent stroke, TIA and vascular death in the present cohort is illustrated in table 1. Evidence of new brain infarction was identified on brain CT of 2.03% patients (8 out of 393) with TIA, 39.8% (47 out of 118) of the patients with MIS, and 46.6% (55 out of 118) of the entire cohort. Duplex ultrasound disclosed symptomatic $\geq 70\%$ extracranial internal carotid artery stenosis in 3.4% (4.118) of the patients with TIA, 3.6% (14 out of 393) patients with MIS, and 3.5% (18 out of 511) patients with minor ischemic event. The effects of 20 evaluated features on recurrence rate of TIA or MIS during 3 days and 3 months follow-up in patients with minor ischemic cerebrovascular events is described in table 2. From the univariate analysis (Table 2), 3 out of the 20 factors were statistically significant for predicting stroke and TIA at 3 days. Crescendo TIAs and multiple TIAs were associated with 5-fold and 4-fold greater risk of stroke in 3 days in a univariate analysis ($\chi^2 = 48.0$, OR = 5.12, 95%CI 3.13-8.35, $P < 0.001$) and ($\chi^2 = 3.98$, OR = 3.98; 95%CI 1.53-10.3, $P = 0.003$), respectively. MIS patients had significantly lower rate of stroke in 3 days comparing to TIA cases; ($\chi^2 = 24.6$, OR = 0.109, 95%CI 0.028-0.289, $P < 0.001$). There was a significant association of 4 evaluated factors with 3 months recurrence of stroke in the univariate analysis (Table 2). Crescendo TIAs and multiple TIAs were associated with 3.7-fold and 3-fold greater risk of stroke in 3 months in a univariate analysis ($\chi^2 = 31.4$, OR = 3.72, 95%CI 2.30-6.0, $P < 0.001$) and ($\chi^2 = 11.97$, OR = 3.08, 95%CI 1.58-5.98, $P < 0.001$), respectively. The ABCD² score is a prognostic system based on clinical data designed to predict stroke risk within 7 days after TIA to guide the triage.¹⁷ The ABCD² score is the most externally validated prediction tool currently available.^{17,18} This score has been independently validated in different clinical settings and is now recommended for use in triaging TIA patients by several major clinical guidelines.^{17,18,20} Among the ABCD² items, only weakness had a significant effect on recurrence of stroke at 3 months; ($\chi^2 = 5.21$, OR = 2.09, 95%CI 1.09-4.01, $P = 0.025$) in univariate analysis. MIS patients had significantly

lower rate of stroke in 3 months comparing to TIA cases; ($\chi^2 = 15.19$, OR = 0.26, 95%CI 0.12-0.53, $P < 0.001$). The association of the 20 factors with stroke and TIA recurrence at 3 days and 3 months in a similar multivariate model of our cohort were separately analyzed in table 3. On multivariate backward logistic regression analysis of the total 511 patients, only index TIA/stroke was significantly associated with 3 days stroke recurrence; (OR = 0.115, 95%CI 0.015-0.898; $df = 1$, $P = 0.039$). In other words, patients with index stroke had 11.5% lower risk of recurrent stroke in 3 days compared patients with index TIA. Weakness was the only factor associated significantly with 3 days TIA recurrence in multivariate analysis of our cohort; (OR = 4.61, 95%CI 1.014-20.97, $df = 1$, $P = 0.048$). This item increased 4.6-fold risk of 3 days TIA in patients with minor ischemic event. Diabetic patients had 2.6-fold more chance of recurrent stroke in 90 days in multivariate analysis of our whole cohort; (OR = 2.65, 95%CI 1.49-6.72, $df = 1$, $P = 0.039$). None of the other evaluated factors had a significant independent influence on stroke recurrence in 3 months follow-up of the study groups. Eleven vascular deaths (4 males, 7 females) occurred during 3 months of follow-up in the whole cohort and 6 vascular deaths happened in 3 days too. Among 20 evaluated factors, only coronary artery disease and atrial fibrillation had a significant association with 3 months vascular death in univariate analysis; ($\chi^2 = 8.91$, OR = 5.48, 95%CI 1.57-19.04, $P = 0.007$) and ($\chi^2 = 18.91$, OR = 10.41, 95%CI 2.86-37.85, $P = 0.002$), respectively. Due to low number of cases with vascular death, logistic regression analysis was not possible for association of 20 factors with vascular death in the present cohort.

Discussion

The 3 days and 3 months rate of recurrent stroke in the whole cohort with TIA or MIS was 20.6% and 23.1%, respectively. A prospective study of 345 TIA patients in Spain was associated with 20% risk of stroke within the next 90 days and half of this

recurrent events occurred in first 3 days.²³ The risk of stroke was 2.5% at 2 days in an Italian study of TIA patients¹⁹ and 11.1% at 90 days in another study in Canada.⁵ 711 patients with TIA or MIS were prospectively recruited from five centers in the UK.¹ Recurrent stroke and TIA occurred in 90 days in 4% and 14% of the cohort respectively.¹ Review of a Canadian stroke registry found that the stroke risk in 30 days after a first TIA was 8%, with half of these strokes occurred within the first 2 days.²⁴ Thirty four percent risk of stroke in 3 days and 36% risk of stroke at 90 days in our TIA patients was much higher than other reported studies.²⁵⁻²⁷ The main reason of this high frequency of recurrent stroke in our patients was diagnosis of index TIA by stroke neurologist which diminished recruiting migraine, seizure and neurotic patients as probable TIA. The main indication for admission of TIA patients in our center was appearance of multiple or crescendo TIAs. This group of TIA patients was more risky than other cases.²⁸ Since 71.2% of our TIA patients had multiple TIAs and TIA cases constituted 76.9% of our whole patients, the high rate of 3 days and 3 months stroke recurrence in our cohort was reasonable. A similar study performed in Spain in patients with TIA or MIS revealed 16.1% rate of 3 months and 9% rate of 7 days recurrent stroke.⁹ This Spanish study did not find any different risk of recurrent stroke between patients with minor stroke compared to patients with TIA.⁹ In a cohort study of TIA or MIS patients in the UK, estimated risk of stroke in 7 days, 30 days and 90 days was higher for MIS than TIA patients.²⁹ In multivariate regression analysis of the present cohort, only index TIA/stroke was associated with a significant effect on recurrence of stroke within 3 days. Stroke as index event had a significantly protective effect on recurrence of stroke and whole ischemic cerebrovascular events in 3 days and 3 months in our patients in univariate analysis. Paradoxically, the risk of a subsequent ischemic stroke may be less after a completed stroke than after a TIA.¹¹

Table 1. Number and percentage of patients with recurrent stroke, transient ischemic attack and vascular death during 3 days and 3 months follow-up of the whole cohort

Index event/ follow up event	3 days stroke	3 days TIA	3 days vascular death	3 months stroke	3 months TIA	3 months vascular death
TIA n = 393	132 (34%)	40 (10.2%)	2 (0.5%)	141 (35.9%)	108 (27.5%)	5 (1.3%)
MIS = 118	7 (5.9%)	37 (31.5%)	4 (3.4%)	29 (24.6%)	71 (60.2%)	6 (5.1%)
Total = 511	104 (20.4%)	41 (8.1%)	6 (1.2%)	117 (22.9%)	99 (19.4%)	11 (2.2%)

TIA: Transient ischemic attack; MIS: Minor ischemic stroke

Table 2. The analyzed factors and their association in the univariate analysis with stroke and transient ischemic attack recurrence in 3 days and 3 months in 505 patients

Analysed Factor (number)	3 days stroke risk		3 days TIA risk		3 days stroke + TIA risk		3 months stroke risk		3 months TIA risk OR		3 months stroke+TIA risk	
	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
Age group \geq 60 (323)	1.242	0.403	0.872	0.734	1.118	0.602	1.183	0.493	0.948	0.899	1.192	0.382
Duration*	-	0.320	-	0.862	-	0.313	-	0.744	-	0.517	-	0.305
Gender (male:315)	0.861	0.554	0.518	0.090	0.705	0.117	1.013	1	0.980	0.358	1.066	0.496
Hypertension (357)	1.436	0.207	1.794	0.156	1.630	0.046	1.506	0.117	1.398	0.282	1.552	0.040
Diabetes (131)	1.431	0.186	1.246	0.574	1.438	0.107	1.484	0.128	1.424	0.206	1.776	0.007
Hyperlipidemia (166)	0.872	0.062	1.298	0.481	0.999	1	0.810	0.408	1.150	0.599	1.025	0.920
Smoking (74)	1.309	0.413	0.820	0.819	1.156	0.667	1.196	0.535	0.823	0.729	0.921	0.792
Atrial fibrillation (30)	0.554	0.446	0.926	1	0.635	0.386	0.321	0.132	0.694	0.782	0.446	0.136
Coronary disease (128)	1.048	0.893	1.536	0.251	1.232	0.409	1.021	1	1.383	0.251	1.094	0.741
Other cardiac disease (13)	0.815	0.139	0.968	1	0.232	0.20	0.791	0.080	0.444	0.702	0.157	0.070
\geq 70% carotid stenosis (18)	0.543	0.548	0.650	1	0.540	0.423	0.749	1	0.650	0.751	0.621	0.713
History of stroke(85)	1.211	0.533	2.717	0.007	1.799	0.028	1.347	0.294	2.041	0.019	1.601	0.072
Index (TIA-Stroke)**	0.109	0.000	1.671	0.170	0.376,	0.001	0.260	0.000	0.747	0.385	0.393	0.000
Weakness (410)	1.963	0.057	5.008	0.020	2.710	0.001	2.098,	0.025	1.817	0.121	2.047	0.006
Speech*** disturbance (113)	0.957	1	2.167	0.703	1.295	0.795	1.234	1	1.126	1	1.289	0.206
Sensory disturbances (313)	1.290	0.353	1.115	0.850	1.271	0.297	1.258	0.375	1.442	0.204	1.324	0.196
Amarosis fugax (10)	1.307	1	1.465	1	1.438	0.702	1.117	1	4.508	0.037	3.988,	0.068
New infarct on CT (55)	0.646	1	0.920	0.641	0.403	0.468	1.307	0.668	0.841	0.617	0.643	0.722
Multiple TIAs**** (280)	3.988	0.003	0.753	0.556	1.760	0.058	3.081	0.000	0.889	0.666	1.723	0.020
Crescendo TIAs**** (108)	5.120	0.000	0.628	0.328	3.363	0.000	3.722	0.000	1.605	0.097	2.963	0.000

*: Duration of symptoms categorized as $<$ 10 minutes (111), 10-59 minutes (133) and \geq 60 minutes (261) in whole of the cohort; TIA: Transient ischemic attack; MIS: Minor ischemic stroke

** : TIA (388) and MIS (117); ***: Speech disturbance without weakness; ****: Analysed in 388 TIA patients

†: Six cases with vascular death at 3 days and 11 cases with vascular death at 3 months were omitted in analysis

Table 3. Factors with influence on recurrence rate of stroke or transient ischemic attack in final step of multivariate backward conditional regression analysis in the whole cohort

Outcome event, analysis in final step	Influencing factor	B	SE	P	OR	95% CI
Recurrence of stroke in 3 days, step (15)	Index TIA-stroke	-2.162	1.048	0.039	0.115	0.015-0.898
	History of stroke	1.048	0.591	0.076	2.853	0.896-9.078
Recurrence of TIA in 3 days, step (16)	Weakness	1.528	0.773	0.048	4.611	1.014-20.979
Recurrence of stroke in 3 months, step (15)	Diabetes Mellitus	0.976	0.474	0.039	2.655	1.049-6.722
	Index TIA-Stroke	-0.955	0.586	0.103	0.385	0.122-1.213
Recurrence of TIA in 3 months, step (15)	Index TIA-Stroke	-7.90	0.482	0.101	0.454	0.177-1.167

TIA: Transient ischemic attack; MIS: Minor ischemic stroke

Thus, patients with index TIA are actually more unstable in terms of a new stroke than those presenting an index stroke¹¹. Increasing number of TIAs in the 3 months before index event TIA was the most significant adverse prognostic factor for recurrent stroke in the UK study.³⁰ Crescendo TIAs was the most significant predictor of subsequent stroke within 90 days (OR = 7.6) independently of other predictors in a Japanese study of TIA patients.³¹ Crescendo TIAs and multiple TIAs were associated with 5-fold and 4-fold increase in stroke risk in 3 days in univariate analysis of our study group. Crescendo TIAs and multiple TIAs were also associated with 3.7-fold and 3-fold greater risk of stroke in 3 months in a univariate analysis of the present cohort. These clinical characteristics of TIA should be considered as indication of urgent admission and therapeutic interventions in TIA patients.²⁸ This finding could reflect an unstable vascular condition with higher risk.⁹ Addition of multiple TIAs to ABCD² score might augment the predictive accuracy.²⁵ Our research work supported adding multiple or crescendo TIA to ABCD² score and giving score of 4 to this clinical item as suggested by North Hertfordshire rapid access TIA service referral form (accessible on-line at: <http://www.enherts-tr.nhs.uk/gps-professionals/files/2010/04/Rapid-Access-TIA-service-referral-form.pdf>). The univariate variables analysis of REACH registry cohort revealed previous history of TIA or stroke, and diabetes as significant risk factors of stroke in a 1-year-follow-up of TIA or MIS patients, $p < 0.01$ and $P = 0.02$, respectively.²⁰ Previous history of stroke had a non-significant effect on recurrence of stroke in 3 days in multivariate analysis of our patients. Previous history of stroke had also a significant effect on recurrence of TIA in 3 months in univariate analysis of our patients. Diabetes had a significant effect on stroke recurrence in 90 days in multivariate model of our cohort. While, none of the other evaluated factors had a significant independent influence on

stroke recurrence in 3 months follow-up of our study group. A population-based study of Alberta TIA patients revealed hypertension, diabetes and older age as predictive of stroke by adjusted risk estimate in one year but not earlier, and the early risk of stroke was not predicted by clinical and demographic factors.³² The Stroke Prognosis Instrument II (SPI-II) designed for TIA and MIS patients in the U.S. and validated by using multiple American and European cohorts.² Prior history of stroke or TIA, coronary artery disease, atrial fibrillation and diabetes were associated with risk of stroke or death during two years in the unadjusted analysis of SPI-II derived cohort.² In multivariate model of SPI-II derived cohort, age > 70 years, prior history of stroke and diabetes were significantly associated with stroke or death in 2 years follow up². Unilateral weakness was the sole ABCD² item associated with 90 days stroke risk in multivariate analysis of patients in Dublin TIA study.³³ Weakness was independently associated with 3 days TIA risk in our TIA group. Diabetes was the only ABCD² item which was independently associated with stroke risk in 3 months in our study group. In the similar Spanish study of patients with TIA or MIS, 3 months stroke recurrence was independently associated with weakness, speech impairment, duration of symptoms, multiple TIAs, heart failure and severe symptomatic arterial stenosis and with 7 days recurrence; they obtained the same independent factors except speech impairment.⁹ The 90-day recurrence of stroke was independently associated with weakness, previous history of TIA and severe symptomatic arterial stenosis in separated groups analysis of Spanish TIA and MIS patients⁹. Hypercholesterolemia and diabetes were independent predictors of stroke risk in 30 days in Greek TIA patients¹². Among subjects with TIA in WASID trial, the presence of cerebral infarct on neuroimaging was the only statistically significant predictor of higher risk of stroke within 90 days (hazard ratio = 4.7).³⁴ Among 4574 TIA

patients, new or old infarction was present in 24% of brain CTs and 28% of DWI.³⁵ New or old infarction was independently predictive of stroke in 7 days; OR = 4.2 for CT and OR = 6.2 for DWI.³⁵ Leukoaraiosis, new and old ischemic changes in CT were associated with 4-fold greater risk of stroke in 30 days in univariate analysis of Italian TIA patients.⁷ New ischemic changes on CT have been shown by Douglas et al. to be predictive of stroke risk (OR = 4; P = 0.028);³⁶ however, this finding was not associated with stroke recurrence in univariate and multivariate analysis of our patients with minor ischemic events. Carotid stenosis was strongly associated with stroke risk in 90 days after TIA; (hazard ratio = 3.3; P = 0.002) in Dublin TIA study.³³ In multivariate analysis of Spanish TIA patients, only large artery occlusive disease remained independent predictor for stroke recurrence in 3 days and 90 days.²⁴ Although symptomatic severe carotid stenosis has been reported as an important predictor of stroke recurrence within 3 months,³⁷ no association was observed between symptomatic severe carotid stenosis and stroke risk in 3 days and 3 months in our study group. The risk of stroke recurrence within a month after cardioembolic TIAs was estimated to be 4.6%.³⁷ This relatively low risk cardioembolic etiology could stem from the fact that all the mechanisms were lumped together while not all the cardiac sources of emboli carry the same risk.³⁷ No association was found between atrial fibrillation and recurrent stroke in 7, 28, or 90 days in Duplin TIA study.³³ No association was found between atrial fibrillation, coronary artery disease and other high risk cardiac source of embolism and stroke risk in 3 or 90 days follow up of our TIA or MIS patients in the present study. Coronary artery disease, atrial fibrillation and other high risk cardiac disease were not significantly associated with 1-year stroke risk in REACH registry.²⁰ Validation of ABCD² scoring systems in our patients was published elsewhere.^{38,39}

Conclusion

Multiple and crescendo TIAs is the main predictive of stroke recurrence, derived in univariate analysis of our patients with minor ischemic events. Patients with index stroke had significantly lower risk of recurrent stroke in 3 days than patients with index TIA. Diabetes was independently associated with 3 months stroke recurrence of our patients with TIA or MIS.

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Conflict of Interests

Authors have no conflict of interests.

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Effects of negative T wave in electrocardiography on prognosis of post-myocardial infarction patients

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Original Article

Abstract

BACKGROUND: Negative T (NT) wave in electrocardiography (ECG) is one of the important factors in determining short- and long-term outcomes in patients with acute myocardial infarction (MI). In this study, we compared clinical and paraclinical findings in post-MI patients according to presence or absence of NT wave.

METHODS: A cross-sectional study was conducted on patients with acute ST elevation MI who presented to Shahid Modares Hospital (Tehran, Iran) during 2009-10. After undergoing streptokinase therapy, demographic characteristics and ECG and exercise test findings of the subjects were compared based on the presence or absence of NT wave.

RESULTS: Overall, 116 patients including 69 cases with NT wave (NT group) and 47 cases without NT wave (PT group) were enrolled (mean age: 53.7 ± 7.1 vs. 54.1 ± 6.8 years old). Mortality rate during the first five days was 13% in the NT group and 29% in the PT group ($P < 0.05$). Ejection fraction values of the NT group were significantly higher than the PT group ($P = 0.005$). However, left ventricular end-diastolic diameter of the NT group was significantly less than the PT group ($P = 0.005$). Moreover, ST segment depression was significantly less frequent in the NT group compared to the PT group.

CONCLUSION: Patients with ST elevation MI accompanying with NT wave in ECG versus have better prognosis and myocardial function than similar patients without NT wave. Therefore, invasive procedures should be recommended for patients without NT wave.

Keywords: Echocardiography, Exercise Test, Myocardial Infarction, Negative T Wave, Echocardiography

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Introduction

Myocardial infarction (MI) is one of the main causes of death and disability worldwide. Despite vast improvements in the areas of prevention, diagnosis, and treatment, it is still considered as a health and medical problem, especially in developed and developing countries.¹ Although mortality rates after MI have reduced about 25-30% during the past two decades, MI is currently the first cause of mortality in western societies.²⁻⁴ Reduced in-hospital mortality rate of patients with MI (from 10.4% in 1994 to 6.3% in 2006) may be a result of advances in immediate diagnostic methods and effective therapeutic interventions.⁵

Various factors including age, sex, Killip class, and history of heart failure have been proposed to affect the prognosis and mortality rate after MI.^{6,7} Electrocardiographic (ECG) changes and exercise test are also among the factors that determine the outcome and short- and long-term prognosis of patients with MI.^{8,9} Various ECG changes, such as ventricular tachycardia and fibrillation, premature ventricular contractions, decreased heart rate variability, delayed potential in ECG signals evaluated with mobile monitoring, prolonged QRS wave, and T wave changes, can influence the prognosis of patients with acute MI.¹⁰⁻¹² Classically but not always accurately, a negative T wave

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represents ischemia and a very long T wave represents MI.¹³ Previous studies on negative T wave after acute MI have not reported clear results about its prognostic role and its relationship with paraclinical findings of patients.^{7,12,14} Therefore, we compared different paraclinical findings of patients with ST segment elevation MI (STEMI) based on the presence or absence of negative T waves.

Materials and Methods

This analytical cross-sectional study was conducted on patients admitted to Shahid Modares Hospital (Tehran, Iran) with the diagnosis of MI during 2009-10. At least two 12-lead ECGs were recorded in all patients during the first 24 hours of hospitalization. Using simple random sampling, patients with confirmed STEMI were enrolled in the study after they had provided informed consent.

Within 24 hours after receiving streptokinase, patients were divided into two groups based on the presence or absence of negative T wave in ECG. Various references have defined negative T wave in a range from 1 to 10 mm. Therefore, in order to be more accurate, negative T wave was accepted when T wave had at least five millimeters from the base point of the line adjacent to the TP segment.^{13,15,16} Patients with heart rhythm disorders (such as atrial flutter and bundle branch blocks) were excluded. All cases of false positive or negative T wave (stroke, re-infarction, ischemia after infarction) were also excluded.

During the first five days after receiving streptokinase, all patients were assessed by ECG and exercise test. The obtained data in the two groups was analyzed and compared using chi-square and student t tests in SPSS for Windows 16.0 (SPSS Inc., Chicago, IL, USA). P values less than 0.05 were considered significant. In cases of significance, odds ratio (OR) was calculated based on 95% confidence interval (CI).

Results

In total, 176 patients were examined and 116 patients with confirmed STEMI were included. Among the 116 patients, 69 patients with MI associated with negative T wave (NT) and 47 patients without negative T wave (PT) were studied (mean age: 53.7 ± 7.1 vs. 54.1 ± 6.8 years old, $P > 0.05$). There was not a significant difference between the two groups in terms of sex distribution (66% male in the PT group vs. 63% in the NT group, $P > 0.05$). Other demographic findings did not indicate significant differences between the two groups, either (Table 1).

The mean elevation of ST segment was 6.1 ± 2.0 mV in the NT group and 5.4 ± 1.8 mV in the PT group ($P < 0.05$). The mortality rate during the first five days after MI was significantly higher in the PT group than in the NT group (29% vs. 13%). This difference was significant despite Yates correction which is the sign of a relationship beyond statistical probabilities. Likewise, the incidence of ventricular tachycardia during the first five days was significantly higher in the PT group than in the NT group (47% vs. 28%) (Table 2).

Table 1. Baseline characteristics of patients with ST segment elevation myocardial infarction (MI)

Variable	NT Group (n = 69)	PT Group (n = 47)	P
Age (years)	53.7 ± 7.1	45.1 ± 6.8	0.450
Gender (male)	44 (63)	31 (66)	0.924
Past history of MI	17(25)	12 (26)	0.613
Diabetes mellitus	46 (67)	33 (70)	0.133
Smoking	43(62)	28 (59)	0.378

NT: Negative T wave in echocardiogram; PT: Positive T wave in echocardiogram

Values are presented as mean \pm SD or n (%)

Table 2. Echocardiographic findings in patients with ST segment elevation myocardial infarction (MI)

Variable	NT Group (n = 69)	PT Group (n = 47)	P
Ejection fraction	38.7 ± 4.8	37.0 ± 4.1	0.005
LVEDD	5.1 ± 3.2	6.3 ± 3.7	0.005
MR Grade 0	12 (20)	7 (20)	> 0.05
MR Grade 1	27 (44)	15 (43)	> 0.05
MR Grade 2	20 (33)	11 (31)	> 0.05
MR Grade 3	2 (3)	2 (6)	> 0.05
Ventricular aneurysm	8 (13)	5 (14)	> 0.05
Thrombosis	3 (5)	2 (6)	> 0.05

NT: Negative T wave in echocardiogram; PT: Positive T wave in echocardiogram; LVEDD: Left ventricular end-diastolic diameter; MR: Mitral regurgitation

Values are presented as mean \pm SD or n (%)

According to ECG findings, the two groups were significantly different in terms of mean ejection fraction and left ventricular end-diastolic diameter. However, no significant differences in various degrees of mitral regurgitation, aneurysm,

and ventricular thrombus were found between the two groups (Table 3).

Exercise test results of patients were evaluated and compared according to ST segment changes and exercise capacity [in metabolic equivalents (METs)] during the test. ST segment depression during the exercise test was not detected in 32% of the NT group and 9% of the PT group ($P < 0.05$). Moreover, 45% of the NT group and 24% of the PT group had 1 mm ST segment depression in the exercise test ($P < 0.001$). In addition, 2 mm ST segment depression was more frequent in the PT group than in the NT group (55% vs. 17%; $P < 0.001$) (Table 3).

Patients with an exercise capacity of more than 6 METs constituted 50% of the NT group and 27% of the PT group ($P < 0.001$). There was a significant difference in prevalence of negative T wave and positive T wave among individuals with exercise capacity of 2-6 METs. However, there was no significant difference between the two groups in patients with exercise capacity of 2 METs (Table 4).

Discussion

According to ECG findings and exercise test results in the present study, cardiac function of patients with MI in the NT group was better than patients in the PT group. Moreover, during a short five-day follow-up period, the mortality rate of the NT group was lower than that of the PT group. Inverted T wave in precordial leads of ECG after ST elevation has long been considered as a symptom of lesions of acute coronary artery stenosis and an indication of the incidence of coronary events and MI.^{17,18} However, recent studies have proposed negative T wave as a more accurate marker of improving myocardial function.^{19,20}

Elhendy et al. showed the positive role of negative T wave in the prognosis of patients with nontransmural MI.¹⁹ Although the mentioned study failed to establish a significant relation between negative T wave and prognosis of transmural MI,¹⁹ it is considered as one of the first studies in this area. Corbalan et al. indicated an association between the presence of negative T wave and lower mortality rate during the first 24 hours after acute

MI in patients who were on thrombolytic therapy.²⁰ While the follow-up period was longer and the sample size was smaller in the present study, we obtained similar results. Ramirez et al. evaluated patients with non-Q wave heart attack after thrombolytic therapy. They reported higher survival rate among individuals with negative T wave than those without it. However, the researchers only assessed survival rate in a longer timeframe, but did not examine the patients in terms of ST segment elevation or ECG and exercise test findings.¹⁷

Although the above-mentioned studies emphasized better survival rate of patients with negative T wave, none of them has considered ECG and exercise test findings as two helpful tests in predicting the prognosis and cardiac function of patients. On the other hand, Kusniec et al.²¹ and Agetsuma et al.²² highlighted the positive role of negative T wave in the prognosis of patients through ECG and paraclinical evaluation. They also suggested higher left ventricular ejection fraction (as an indicator of cardiac pump function) in patients with MI and negative T wave compared to those without negative T wave. These findings are not consistent with the results of the present study. This inconsistency may be justified by not excluding false positive cases of negative T wave and also considering deep form of negative T wave in the two mentioned studies. Nevertheless, studies with larger sample size and more accurate sampling seem more logical. Moreover, Karadede et al. stated that patients with STEMI and positive T wave had a worse response to dobutamine stress test.²³ Although we found different results about ejection fraction, their provocation test results were in accordance with our exercise test findings.

Previous studies have also considered negative T wave a sign of good patency of the involved vessel.^{24,25} According to the results of the present study, other signs of myocardial performance (except left ventricular end-diastolic diameter) were better in the NT group than in the PT group. It can hence be concluded that reperfusion changes the process of infarction and electrical potentials and causes the incidence of negative T wave.^{24,25}

Table 3. ST segment elevation in the groups with negative T wave (NT) and positive T wave (PT)

ST segment elevation	PT (n = 33)	NT (n = 60)	Odds Ratio	P
No	3 (9)	19 (32)	1.3	0.020
1 mm	8 (24)	27 (45)	0.87	0.001
2 mm	18 (55)	10 (17)	1.71	0.001
> 2 mm	4 (12)	4 (7)	0.37	> 0.05

Values are expressed as n (%)

Table 4. Exercise capacity of the participants in submaximal exercise tolerance test in groups with negative T wave (NT) and positive T wave (PT)

Exercise capacity (METs)	PT (n = 33)	NT (n = 60)	Odds ratio	P
2	6 (18)	4 (7)	1.88	> 0.05
2-4	12 (36)	5 (8)	1.78	0.001
4-6	6 (18)	21 (35)	0.88	0.005
6	9 (27)	30 (50)	0.93	0.005

METs: Metabolic equivalents
Values are expressed as n (%)

Szydlo et al. demonstrated greater interruption of blood supply and longer repolarization duration in the group of patients with acute STEMI without negative T wave than subjects with negative T wave. These factors may provoke arrhythmias and sudden death despite similar ECG findings in the two groups (which is in contrast with the present study).²⁵

Ando et al. reported the risk of in-hospital death after MI to be three times higher in patients with negative T wave in previous ECG than in those without a similar history.²⁶ This finding is inconsistent with ours probably because Ando et al. only evaluated negative T wave in previous ECG of patients.²⁶

With advances in techniques of reperfusion, the role of ECG findings in selecting patients and determining the success rate after intervention has received more attention. Sorensen et al. showed significantly lower delayed microvascular reperfusion in patients with STEMI and negative T wave than patients with positive T wave.²⁷ This specifies the importance of negative T wave in predicting recovery after MI. In a study on patients after STEMI, Altun et al. demonstrated that normalization of negative T wave is a stronger predictor of viability and consequently myocardial performance in myocardial perfusion single-photon emission computed tomography (SPECT) than negative T wave itself.²⁸ Therefore, not only the presence of negative T wave, but also alternations in T wave (especially toward its negative) have been particularly proposed as prognostic factors for survival of in patients with some degrees of ventricular failure due to cardiac ischemia.^{29,30} However, further studies in this regard are warranted.

Conclusion

Based on our findings and previous studies, it can be concluded that prognosis and myocardial tissue performance of patients with STEMI with negative T wave in the initial ECG are more favorable than patients without negative T wave. Thus, more accurate and aggressive follow-up for patients without negative T wave seems to be necessary.

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Conflict of Interests

Authors have no conflict of interests.

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Corrected thrombolysis in myocardial infarction frame count and ejection fraction in patients undergoing primary percutaneous coronary intervention for myocardial infarction

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Original Article

Abstract

BACKGROUND: This study aimed to assess the associations between corrected thrombolysis in myocardial infarction frame count (CTFC) of the infarct-related artery (IRA) and ejection fraction (EF) after three-six months in patients who underwent primary percutaneous coronary intervention (PPCI) for ST segment elevation myocardial infarction (STEMI).

METHODS: CTFC was determined by a digital system for 78 patients. EF was measured through Simpson's method upon discharge and three-six months later. The subjects were divided into two groups of CTFC \leq 20 (n = 54) and CTFC $>$ 20 (n = 24). Association between CTFC and EF were then specified.

RESULTS: CTFC \leq 20 and CTFC $>$ 20 were present in 69.2% and 30.8% of the patients, respectively. There was no significant difference between the two groups regarding baseline characteristics. EF at the time of discharge was $42.1\% \pm 10.2\%$ and $43.5\% \pm 11.4\%$ in groups with CTFC \leq 20 and $>$ 20, respectively. There was no significant association between EF at discharge and CTFC (P = 0.611). After three months, EF changed to $49.6\% \pm 8.7\%$ and $41.6\% \pm 12.4\%$ in the groups with CTFC \leq 20 and CTFC $>$ 20, respectively. Three months after PPCI, EF and CTFC had a significant relation (P = 0.007). Cumulative number and percentage of shock and death were 3 (3.8%) and 2 (2.6%), respectively.

CONCLUSION: Lower CTFC of the infarct-related artery in patients undergoing PPCI for STEMI was associated with higher left ventricular ejection fraction after three months.

Keywords: Corrected Thrombolysis in Myocardial Infarction Frame Count, Ejection Fraction, Percutaneous Coronary Intervention, Myocardial Infarction

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Introduction

ST segment elevation myocardial infarction (STEMI) is a major health problem whose rate increases with increasing age in both sexes. Primary percutaneous coronary intervention (PPCI) is an urgent angiographic strategy following angioplasty with or without stenting. It is accepted as the preferred reperfusion strategy performed in many cases with STEMI.¹

The thrombolysis in myocardial infarction (TIMI) flow grading system is a qualitative method for measuring reperfusion strategy. On the other hand, the corrected TIMI frame count (CTFC) is a quantitative method to assess the TIMI flow grading system. It is simply performed by counting the number of angiographic frames elapsed until the

contrast material arrives in the distal bed of the vessel of interest. The mean CTFC of normal coronary arteries has been reported as 21.1 ± 1.5 for left anterior descending artery (LAD), 22.2 ± 4.4 for left circumflex artery (LCX), and 20.4 ± 3.3 for right coronary artery (RCA).^{1,2} CTFC is an independent predictor of in-hospital mortality following STEMI.³⁻⁶

The objective of this study was to evaluate the associations between CTFC and ejection fraction (EF) soon after PPCI and three-six months later in patients with STEMI. As EF is a known predictor of early and late survival, the findings of the current study may enable cardiologists to better predict cardiovascular outcomes following PPCI in patients with STEMI.

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Materials and Methods

In 2009, this prospective study was conducted on patients who had received PPCI within 12 hours from the diagnosis of STEMI. Overall, 78 patients, including 66 (84.6%) men and 12 (15.4%) women, were included. STEMI was defined as typical chest pain and the presence of electrocardiographic criteria.⁷ Patients who had undergone rescue percutaneous coronary intervention (PCI) or late PCI were not included.

A checklist about cardiovascular risk factors, physical examination on admission, door-to-balloon time, systolic blood pressure, location of myocardial infarction (MI), TIMI flow grade, CTFC, ST resolution, EF (upon discharge and after three-six months), and in-hospital adverse events was filled out for all patients. Door-to-balloon time was defined as the interval between arrival to the hospital and the use of a therapeutic device (thrombectomy catheter, balloon, and stent).

All patients received 325 mg of aspirin, 300-600 mg of clopidogrel, and 40 mg of atorvastatin. PPCI was performed in the presence of reduced TIMI flow grade (< 3), occluded infarct-related artery, and/or a culprit lesion stenosis of > 50%. The use of glycoprotein IIb/IIIa inhibitors, thrombectomy and bare-metal or drug-eluting stents was left to the decision of the interventionalist.

Angiography CDs of the patients were reviewed by two interventional cardiologists and TIMI frame count (TFC) was measured by a digital system in the catheterization laboratory. TFC is the number of cine-frames required for contrast to reach a standardized distal coronary landmark in the culprit vessel and was determined by a previously suggested method.^{3,8} The first frame was selected when the column of the contrast extended across > 70% of the arterial lumen with antegrade flow.⁹ The reported number was based on a cine filming rate of 30 frames per second. The last frame is a distal landmark to which the contrast enters. Distal landmark in the RCA is the first branch of the posterolateral extension of the RCA after the origin of the posterior descending artery. In the circumflex artery, it is the most distal branch of the obtuse marginal branch which included the culprit lesion. In the left anterior descending artery, it is a distal bifurcation which is usually placed at the apex of the heart. CTFC means that the TFC for LAD must be corrected by dividing it into 1.7 due to the longer length of the LAD.

Electrocardiograms were recorded on arrival and 60 minutes after the angioplasty. ST resolution was measured 60 minutes after PPCI at the

corresponding lead with maximal ST elevation in pre-PCI echocardiography.

Patients were requested to come back to the hospital three-six months later for the second echocardiography. Patients' EF was measured with biplane Simpson's method upon discharge and after three-six months. Standard medical treatment comprised aspirin, clopidogrel, beta-blockers, atorvastatin, and enalapril/losartan for all patients.

Baseline characteristics were expressed as mean \pm standard deviation (SD) or percentages. Continuous variables were compared by the Student's t-test. Categorical variables were contrasted by the chi-square test (or Fisher's exact test as needed). All analyses were performed with SPSS for Windows 16.0 (SPSS Inc., Chicago, IL, USA). P values less than 0.05 were considered significant.

Results

The patients were divided into two groups of CTFC \leq 20 and CTFC > 20. Table 1 presents baseline characteristics of the studied population stratified by CTFC. There was not any significant difference between the two CTFC groups regarding baseline characteristics.

Table 2 compares the clinical characteristics of the patients. The mean door-to-balloon time in the groups with CTFC \leq 20 and CTFC > 20 was 45.1 ± 16.8 and 44.6 ± 11.8 minutes, respectively ($P = 0.879$). The mean systolic blood pressure/mean diastolic blood pressure in the mentioned groups was $118.5 \pm 20.2/72.3 \pm 12.0$ and $113.7 \pm 22.4/69.6 \pm 10.8$ mmHg, respectively ($P > 0.05$). Less than 10% of the patients in every group had signs of heart failure at presentation. Moreover, there was no significant differences between the two CTFC groups regarding clinical characteristics.

The two CTFC groups were similar in the administration of aspirin, clopidogrel, heparin, glycoprotein IIb/IIIa inhibitors, and atorvastatin. According to angiography results, in the groups with CTFC \leq 20 and CTFC > 20, 16.7% and 4.2% of patients had single vessel disease (SVD), 57.4% and 41.7% had two-vessel disease (2VD), and 25.9% and 54.2% had three-vessel disease (3VD), respectively. Number of narrowed coronary arteries in the two groups did not have a significant difference ($P = 0.036$). Furthermore, stenotic lesions in the LAD were detected in 87.0% and 37.5% of the groups with CTFC \leq 20 and CTFC > 20, respectively. The corresponding rates of stenotic lesions in the LCX were 1.9% and 25.0%. Stenotic lesions in the RCA were also found in 11.1% of

patients with CTFC ≤ 20 and 37.5% of patients with CTFC > 20 ($P < 0.001$ for all). The most infarcted arteries were LAD in patients with CTFC ≤ 20 and

both LAD and RCA in patients with CTFC > 20 . The two groups had a significant difference in pre-PCI TIMI flow grade ($P = 0.006$) (Table 3).

Table 1. Baseline characteristics of patients with ST segment elevation myocardial infarction stratified by post-primary percutaneous coronary intervention (PCI) corrected thrombolysis in myocardial infarction frame count (CTFC)

Variables	Total	Post-PCI CTFC		P
		≤ 20	> 20	
Number	78	54	24	-
Age (years; mean \pm SD)	58.7 \pm 9.2	58.2 \pm 9.3	59.9 \pm 9.1	0.451
Gender (female)	12 (15.4)	10 (18.5)	2 (8.3)	0.324
Obesity	19 (24.4)	15 (27.8)	4 (16.7)	0.395
Family history of coronary artery disease	10 (12.8)	7 (13)	3 (12.5)	1.000
Smoker	34 (43.6)	21 (38.9)	13 (54.2)	0.227
Hypertension	29 (37.2)	19 (35.2)	10 (41.7)	0.619
Hyperlipidemia	27 (34.6)	15 (27.8)	12 (50.0)	0.073
Diabetes mellitus	24 (30.8)	14 (25.9)	10 (41.7)	0.191
Chronic lung disease	0 (0.0)	0 (0.0)	0 (0.0)	-
Cerebrovascular disease	0 (0.0)	0 (0.0)	0 (0.0)	-
Peripheral vascular disease	0 (0.0)	0 (0.0)	0 (0.0)	-
Previous congestive heart failure	0 (0.0)	0 (0.0)	0 (0.0)	-
Previous myocardial infarction	4 (5.1)	2 (3.7)	2 (8.3)	0.583
Previous PCI	5 (6.4)	4 (7.4)	1 (4.2)	1.000
Previous coronary artery bypass grafting	0 (0.0)	0 (0.0)	0 (0.0)	-
Creatinine (mg/dL; mean \pm SD)	1.2 \pm 0.3	1.2 \pm 0.3	1.2 \pm 0.3	0.662

Values are presented as n (%) unless otherwise expressed

Table 2. Clinical and medicine-related characteristics of patients with ST segment elevation myocardial infarction stratified by post-primary percutaneous coronary intervention (PCI) corrected thrombolysis in myocardial infarction frame count (CTFC)

Variables	Total	Post-PCI CTFC		P
		≤ 20	> 20	
Door-to-balloon time (minutes; mean \pm SD)	44.9 \pm 15.4	45.1 \pm 16.8	44.6 \pm 11.8	0.879
Door-to-balloon time ≥ 60 minutes	5 (6.4)	3 (5.5)	2 (8.3)	-
Door-to-balloon time ≥ 90 minutes	0 (0.0)	0 (0.0)	0 (0.0)	-
Systolic blood pressure (mmHg; mean \pm SD)	117.0 \pm 20.9	118.5 \pm 20.2	113.7 \pm 22.4	0.377
Diastolic blood pressure (mmHg; mean \pm SD)	71.5 \pm 11.6	72.3 \pm 12.0	69.6 \pm 10.8	0.325
Signs of heart failure at presentation				
S3	4 (5.1)	2 (3.7)	2 (8.3)	0.583
No rales	69 (88.5)	48 (88.9)	21 (87.5)	
Rales up to 1/3	7 (9.0)	6 (11.1)	1 (4.2)	0.067
Rales more than 1/3	2 (2.6)	0 (0.0)	2 (8.3)	
Cardiac markers (mean \pm SD)				
Troponin (ng/ml)	12.7 \pm 9.4	13.8 \pm 9.6	10.3 \pm 8.7	0.118
Creatine phosphokinase (U/l)	3711 \pm 3706	3603 \pm 2859	3955 \pm 5202	0.757
Creatine kinase MB (U/l)	370 \pm 386	406 \pm 440	288 \pm 209	0.114
Drugs				
Aspirin	24 (100)	24 (100)	24 (100)	-
Clopidogrel	24 (100)	24 (100)	24 (100)	-
Unfractionated heparin	24 (100)	24 (100)	24 (100)	-
Glycoprotein IIb/IIIa inhibitors	63 (80.8)	44 (81.5)	19 (79.2)	1.000
Integrilin	60 (76.9)	42 (77.0)	18 (75.0)	0.928
Tirofiban	3 (3.8)	2 (3.7)	1 (4.2)	1.000
Statin	78 (100)	54 (100)	24 (100)	-

Values are presented as n (%) unless otherwise expressed

SD: Standard deviation

Table 3. Incidence of events in patients with ST segment elevation myocardial infarction stratified by post-primary percutaneous coronary intervention (PCI) corrected thrombolysis in myocardial infarction frame count (CTFC)

Variables	Overall	Post-PCI CTFC		P
		≤ 20	> 20	
Number of narrowed coronary arteries				
1	10 (12.8)	9 (16.7)	1 (4.2)	0.036
2	41 (52.6)	31 (57.4)	10 (41.7)	
3	27 (34.6)	14 (25.9)	13 (54.2)	
Infarct-related artery				
Left main	0 (0.0)	0 (0.0)	0 (0.0)	< 0.001
Left anterior descending	56 (71.8)	47 (87.0)	9 (37.5)	
Left circumflex	7 (9.0)	1 (1.9)	6 (25.0)	
Right coronary artery	15 (19.2)	6 (11.1)	9 (37.5)	
Saphenous vein graft	0 (0.0)	0 (0.0)	0 (0.0)	
Pre-PCI TIMI flow grade of the infarct-related artery				
0	53 (67.9)	38 (70.4)	15 (62.5)	0.006
1	8 (10.3)	8 (14.8)	0 (0.0)	
2	14 (17.9)	5 (9.3)	9 (37.5)	
3	3 (3.8)	3 (5.6)	0 (0.0)	
Stent implantation				
No stents	2 (2.6)	0 (0.0)	2 (8.3)	0.067
One stent	66 (84.6)	48 (88.9)	18 (75.0)	
Two stents	9 (11.5)	6 (11.1)	3 (12.5)	
Three stents	1 (1.3)	0 (0.0)	1 (4.2)	
Drug eluting stent	29 (37.2)	26 (48.1)	3 (12.5)	< 0.001
Stent diameter (mm; mean ± SD)	2.9 ± 0.3	2.9 ± 0.3	2.8 ± 0.3	0.474
Stent length (mm; mean ± SD)	24.7 ± 5.3	25.7 ± 5.0	22.0 ± 5.3	0.007
Intra-aortic balloon pump	3 (3.8)	2 (1.9)	1 (8.3)	0.223
Thrombectomy	3 (3.8)	1 (1.9)	2 (8.3)	0.223
Stent thrombosis	1 (1.3)	1 (1.9)	0 (0.0)	1.000
Cardiogenic shock	3 (3.8)	3 (5.6)	0 (0.0)	0.549
No ST resolution	4 (5.1)	2 (3.7)	2 (8.3)	0.583
In-hospital events				
Major bleeding	0 (0.0)	0 (0.0)	0 (0.0)	-
Stroke/transient ischemic attack	0 (0.0)	0 (0.0)	0 (0.0)	-
Dialysis	2 (2.6)	0 (0.0)	2 (8.3)	> 0.05
Death	2 (2.6)	2 (3.7)	0 (0.0)	1.000

Values are presented as n (%) unless otherwise expressed
SD: Standard deviation

Table 4. Post-primary percutaneous coronary intervention (PCI) corrected thrombolysis in myocardial infarction frame count (CTFC) and ejection fraction (EF) before discharge and three months after discharge

Variables	Overall	Post-PCI CTFC		P
		≤ 20	> 20	
EF before discharge (%; mean ± SD)	42.5 ± 10.5	42.1 ± 10.2	43.5 ± 11.4	0.611
EF after three months (%; mean ± SD)	47.1 ± 10.6	49.6 ± 8.7	41.6 ± 12.4	0.007
EF ≥ 50% before discharge	29 (37.2)	18 (33.3)	11 (45.8)	0.319
EF ≥ 50% after three months	44 (57.9)	34 (65.4)	10 (41.7)	0.079
EF change (%; mean ± SD)	4.2 ± 8.9	7.0 ± 8.3	-1.9 ± 6.9	< 0.001

Values are presented as n (%) unless otherwise expressed
SD: Standard deviation

Stenting was performed for all patients in the group with CTFC ≤ 20 . In the other group, however, two subjects (8.3%) underwent balloon angioplasty without stenting. Drug-eluting stents were used for 48.1% of the patients in the group with CTFC ≤ 20 and for 12.5% of other patients ($P < 0.001$). Two patients (3.7%) in the group with CTFC ≤ 20 and two (8.3%) in the group with CTFC > 20 had no ST resolution ($P = 0.583$) (Table 3).

The use of the intra-aortic balloon pump and thrombectomy devices was low in both groups and without a significant difference. Acute in-stent thrombosis occurred in one patient who underwent coronary artery bypass graft surgery. The rate of cardiogenic shock and death were 5.6% and 3.7% in the group with CTFC ≤ 20 , respectively. The corresponding values in the group with CTFC > 20 were 0% and 0%, respectively. No significant differences were identified between the two groups ($P > 0.05$) (Table 3).

Table 4 compares CTFC and EF before discharge and after three months of treatment. No significant difference was observed for EF at discharge between the two CTFC groups ($P > 0.05$). However, the two groups significantly differed in EF after three-six months. After three-six months, the mean EF was $49.6\% \pm 8.7\%$ and $41.6\% \pm 12.4\%$ in patients with CTFC ≤ 20 and CTFC > 20 , respectively ($P = 0.007$).

Discussion

According to the obtained results, lower CTFC was associated with higher EF after three-six months. CTFC is a quantitative and reproducible method for assessment of infarct-related artery flow. EF is the most powerful determinant of survival. We measured EF a few months after MI when myocardial stunning was likely to resolve.

Research has shown lower CTFC of the infarct-related artery immediately after PCI to be associated with better improvement in left ventricular function.^{10,11} CTFC also has a significant correlation with wall motion score index.¹⁰ Gibson et al. suggested higher CTFC 90 minutes after thrombolytic therapy to be linked with higher adverse outcomes.¹¹ In another study, Gibson et al. reported that patients with acute coronary syndrome who died after PCI had a higher CTFC compared to those who survived.¹² On the other hand, some studies have failed to identify any relations between CTFC and adverse clinical outcomes or functional recovery after thrombolytic therapy.^{13,14}

French et al. found a significant correlation between CTFC and three-week survival after MI. They concluded that CTFC ≥ 40 is a predictor of adverse outcomes including mortality, 30-day in-hospital major adverse cardiac events, reinfarction, congestive heart failure, and left ventricular remodeling.⁶ Gibson et al. detected a weak correlation between CTFC and radionuclide left ventricular EF measured through ventriculography.¹¹

In this study, baseline and clinical characteristics were similar to recently published studies in the field of MI. Like the finding of Nielsen et al. door-to-balloon time was short.¹⁵ Success rate of primary PCI was high, and the presence of CTFC ≤ 20 immediately after PPCI could be a predictor of high EF in patients with STEMI three months after the procedure.

Study limitations

There are several limitations in the current study. First, the number of patients was relatively small. Second, patients referred for primary PCI might have had different LAD length; and a factor of 1.7 to correct the TFC for all of them is not perfect.⁹ Third, the follow-up period was short and hence further studies with longer follow-up are recommended. This allows for better understanding of the role of CTFC in predicting EF and prognosis of patients who undergo PPCI for STEMI.

Conclusion

Lower CTFC of infarct-related artery is associated with better EF after a few months in patients who receive PPCI for STEMI. Post-PPCI CTFC may be an independent predictor of clinical and functional outcome and can thus provide better risk assessment and triage in such patients.

Conflict of Interests

Authors have no conflict of interests.

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The association between dietary intake of white rice and central obesity in obese adults

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Original Article

Abstract

BACKGROUND: Obesity has become one of the most important and the fastest growing health and nutritional problem, not only in developed but also in developing countries. White rice consumption causes an increase in postprandial blood glucose and could be a probable reason for obesity. This study was conducted to investigate the association between intake of white rice and central obesity in an Iranian population.

METHODS: In the present cross-sectional study, a total of 212 subjects were selected based on convenience non-random sampling procedure. Expert interviewers collected socio-demographic and dietary intake data by a face to face method.

RESULTS: We failed to find any significant association between frequency of white rice consumption and body mass index or waist circumference, neither in crude model nor in adjusted models.

CONCLUSION: Although there was no significant association between white rice intake and obesity factors in our study, more studies are necessary with larger population and better design.

Keywords: White Rice, Body Mass Index, Central Obesity, Diet

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Introduction

In recent years, obesity has become one of the most important and the fastest growing health and nutritional problem not only in developed but also in developing countries.¹ WHO anticipated that globally by 2015, around 700 million adult would be clinically obese and 2.3 billion would be overweight.² In Iran the prevalence of weight problems [Body mass index (BMI) > 25] was 63.9% in women and 49.7% in men.³ Obesity as a situation with excess body fat and raise in adipose tissue mass causes several health problem and metabolic diseases.⁴ Individuals with BMI > 25 are considered as overweight and people who have BMI > 30 are considered obese. But BMI does not provide any information about proportion of fat, bone and muscle mass or body fat distribution. However, recent studies have revealed that abdominal fat is more important in prediction of metabolic diseases than subcutaneous fat.^{5,6} Furthermore, central obesity is more closely associated with all cancers,

cardiovascular risk and metabolic disorders such as hypertension, hyperlipidemia and diabetes.⁷ Some studies have reported that waist circumference measurement for central adiposity is very specific and sensitive.^{8,9} Although there are some sophisticated techniques for assessment of central obesity, waist circumference measurement as an anthropometric indicator, is a simple easy to use and low cost method for evaluation of abdominal fat in epidemiological studies.^{8,10}

Dietary factors are associated with overweight and obesity; therefore, dietary intervention could be a target for obesity prevention.^{11,12} High consumption of fiber which is found in fruit, vegetable and grain has important role in dietary interventions.¹³ Previous studies showed that high consumption of whole grain in the diet, lead to lower energy intake, decrease hunger and raise satiety.^{14,15} However, most of the grains are consumed after removing the outer layers and just starch rich endosperm remains. While whole grains

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consumption is associated with a reduction in developing many metabolic diseases such as diabetes,¹⁶ cardiovascular disease,¹⁷ stroke¹⁸ and cancers,¹⁹ refined grains because of their high amount of carbohydrates at least partly are responsible for current obesity problem.¹⁵ Carbohydrate as the most important source of energy in the diet associated with postprandial blood glucose. Glycemic index (GI) shows the ability of carbohydrate foods in raising the postprandial blood glucose.²⁰ Consumption of low GI foods contributes to reduce body fat and control obesity.^{21,22} However, there are some dissimilar results.^{23,24}

White rice consumption causes an increase in postprandial blood glucose as compared with brown rice. In Iranian diet, white rice is one of the most important sources of energy and carbohydrate.²⁵ Previous studies in Iran investigated the association between whole grain consumption and metabolic syndrome²⁶ but most of the studies have done on western population which is different in genetic or life style. To the best of our knowledge there is no study on white rice consumption and central obesity in Iranian population. Hence, the study aimed to explore the association between intake of white rice and central obesity in an Iranian population.

Materials and Methods

Study Population

We conducted a cross-sectional study concerning obese or overweight Iranian adults (BMI > 25) who were visited in Salamt clinic in 2009. People with insufficient information about socio-demographic data, family history, or dietary records were excluded from this survey. A sum of 212 men and women aged 18 to 56 years were selected based on convenience non-random sampling procedure. After explanation of the study protocol for participants, each one was asked to sign the consent form.

Assessment of variables

In a face-to-face method, expert interviewers collected socio-demographic characteristics including age, education and income, medical

history, smoking habits and medication use. Weight and height measurement was completed in barefoot and light clothes. Participants' height measurement was done by a fixed metal ruler to the nearest 0.1 cm and weight measurement was done by a digital scale to the nearest 0.1 kg. BMI was calculated as a measure of obesity, and waist circumference was measured as a central obesity indicator. BMI was calculated as weight (kg) divided by height square (m²). WC was measured horizontally between the iliac crest and lowest rib margin and hip circumference was measured at the maximum protrusion. Waist to hip ratio (WHR) was calculated as WC (cm) divided by hip circumference (cm). Dietary intake of study participants was evaluated with food frequency questionnaire (FFQ).

Statistical methods

For all statistical analyses, SPSS for Windows (version 15; SPSS Inc., Chicago, IL., USA) was used. To compare means of continues variables between white rice consumption groups we applied Student's t-test and for categorical variables chi-square test was used. Linear regression was employed to discover the associations between white rice consumption and obesity factors in different models. In first model, the association was adjusted for age, sex and in the second model further adjustment was done for dietary intake.

Results

Table 1 shows the characteristic of study population separated by frequency of white rice consumption per week. There was no difference in age, sex and adiposity indicators between people who consumed white rice less than 7 times per week and those who consumed more than 7 times per week. Comparison of other dietary factors such as fruit, vegetable, dairy and pulses was not different between two groups.

Multivariate adjusted regression models for obesity indicators and frequency of white rice consumption per week are presented in table 2. We did not find any significant association between frequency of white rice consumption and BMI or central obesity in crude model or in adjusted models.

Table 1. Characteristic of study population separated by frequency of white rice consumption per week

	Less than 7 time per week	More than 7 time per week	P
Age (years)	38.3 ± 14.4	32.2 ± 11.2	0.001
Female (%)	66.9	59.6	0.095
Smoking (%)	9.3	8.9	0.122
Weight (kg)	78.3 ± 16.7	76.4 ± 20.3	0.477
Body mass index (kg/m ²)	30.1 ± 6.4	29.0 ± 8.3	0.353
Waist circumference (cm)	88.4 ± 14.1	85.0 ± 15.8	0.182
Waist to hip ratio	0.82 ± 0.07	0.81 ± 0.07	0.284

Table 2. Multivariate adjusted regression for obesity factors and frequency of white rice consumption per week

	Less than 7 time per week	More than 7 time per week*	P
Weight (kg)			
Crude	1.00	-0.049 (-7.042–3.328)	0.481
Model 1	1.00	-0.001 (-5.030–4.972)	0.991
Model 2	1.00	0.052 (-3.341–7.240)	0.468
Body mass index (kg/m²)			
Crude	1.00	-0.071 (-3.131–1.004)	0.312
Model 1	1.00	0.000 (-1.970–1.967)	0.999
Model 2	1.00	0.042 (-1.464–2.732)	0.552
Waist circumference (cm)			
Crude	1.00	-0.112 (-8.564–1.637)	0.182
Model 1	1.00	-0.025 (-5.541–4.003)	0.750
Model 2	1.00	-0.017 (-5.873–4.786)	0.840
Waist to hip ratio			
Crude	1.00	-0.090 (-0.036–0.011)	0.284
Model 1	1.00	-0.018 (-0.025–0.020)	0.824
Model 2	1.00	-0.028 (-0.028–0.020)	0.745

* B (95% confidence interval)

Model 1: Adjusted for age, sex

Model 2: Adjusted for age, sex and dietary intake

Discussion

In this cross-sectional study, we failed to find any association between frequency of rice consumption and body weight, BMI or central obesity. Rice is a staple food widely used in the world, especially in the eastern countries and Iran. It is an important source of carbohydrate, protein, minerals and vitamins. Recently, most of the rice has been processed and refined. During refining process, bran and germ are removed and just starchy endosperm remains in white rice.

Whole grains because of having some biological active elements including dietary fiber, vitamin E, folate, magnesium and other elements are the main components for a healthy diet.²⁷ In contrast, refined-grains, due to removing of these elements, are typically rich in energy and poor in nutrient content, which are accused for increasing the risk of chronic disease and obesity.²⁸ Refining grains changes the value of the carbohydrates to a higher GI and GL (Glycemic load). Previous studies proposed that rapid absorption of glucose after consumption of high GI foods could lead to a sharp raise in blood glucose and insulin level, thus, glucose enters the body tissues, inhibits lipolysis and induces lipogenesis and obesity.²⁹⁻³¹

In line with some of the previous studies, white rice consumption was not associated with obesity factors in the current study. A prospective study did not find any difference in weight gain as a result of consumption of whole or refined grain breakfast.¹⁴ Another study showed that rice intake with reference

to other carbohydrate sources had lower potential to increase in postprandial glucose.³² Moreover no association was found between metabolic risk factors and refined grain consumption.³³ However, these findings conflict with studies that showed dietary pattern that include white rice may be associated with obesity³⁴ and intake of refined-grain foods was positively related to weight gain¹⁵ and higher visceral adipose tissue.³⁵ On the other hand, another study recently revealed that rice intake was inversely associated with weight gain.³⁶

This discrepancy could be explained by the different source of refined-grains. In Vietnamese, the GI of white rice was reported from 86 to 109 but a review article indicated that the mean GI for white rice was 64.³⁷ A probable reason for finding no association between obesity factors and white rice in the current study could be explained by the GI of Iranian rice. Previous investigations showed that there are some kinds of Iranian rice with low GI (44 ± 9 for Binam rice³⁸ and 52.2 ± 5.1 for Sorna pearl rice³⁹). They supposed that the amylase content of Iranian rice was the reason for the low GI of this rice.³⁸

Another reason for these results could be explained by some studies indicated that rice protein possesses an important function in the triglyceride metabolism, that may improve body weight and adiposity,⁴⁰ so it could reduce the negative effect of high GI rice.

In this study we should consider several limitations. First, this study with a cross-sectional

design was not appropriate to conclude about causality. A further longitudinal study is necessary for stronger conclusion. On the other hand, we used a self reported qualitative FFQ for dietary intake, so we could not estimate the energy intake and it has been reported that obese individuals would like to underreport their dietary intake.⁴¹

In conclusion, although there was no significant association between white rice intake and obesity factors in our study, more studies are necessary with larger population and better design.

Conflict of Interests

Authors have no conflict of interests.

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Postoperative cardiac arrest in children with congenital heart abnormalities

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Original Article

Abstract

BACKGROUND: The exact survival rates and markers of survival after postoperative cardiac arrest in children with congenital heart abnormalities are unknown.

METHODS: In this one-year study, we identified children younger than seven years of age with postoperative cardiac arrest in our pediatric cardiac intensive care unit database. Parameters from perioperative, pre-arrest, and resuscitation periods were analyzed for these patients. Comparisons were made between survivors and non-survivors after cardiopulmonary resuscitation (CPR). Fisher's exact, Student's t, and chi-square tests were used to analyze data.

RESULTS: Of 529 evaluated children who underwent corrective heart surgery, 59 (11%) sustained a documented cardiac arrest. Of these, 22 (37%) survived and regained their vital signs. Perioperative parameters (age, weight, and duration of cardiopulmonary bypass pumping), ventricular physiology, oxygen saturation, and bicarbonate concentration did not influence the outcome of CPR. Greater use of inotropic agents was not associated with higher mortality. A significant relationship was seen between having history of cardiac arrest and CPR success ($P < 0.001$).

CONCLUSION: CPR had undesirable outcomes in patients with hemodynamic dysfunction (i.e. low mean arterial blood pressure). Patients with univentricular physiology or history of cardiac arrest are not prone to a higher risk of mortality following arrest.

Keywords: Cardiac arrest, Congenital, Cardiopulmonary resuscitation, Pediatrics, Operation

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Introduction

The rate of cardiac arrest in the U.S. is approximately 150000 cases per year. While about 10000 of these individuals die, 90000 cases have to continue their lives with cardiac complications. Children with known cardiac diseases, e.g. hypertrophic cardiomyopathy, anomalous coronary arteries, and severe aortic stenosis, may experience cardiac arrest during exercise.¹⁻⁴

Cardiac arrest in admitted children is one of the uncommon yet worrying events. Owing to advancements in cardiopulmonary resuscitation (CPR) and experienced treatment teams, many patients with cardiac arrest, even in the most fatal cases, have survived and returned to life. After surgery, children with congenital heart diseases spend a critical period of time in pediatric cardiac intensive care unit in order for their hemodynamic status to be stabilized. Early prevention and treatment of cardiac arrest during this period are of very high importance. Identifying cardiac arrest

markers and CPR success can lead to reduced mortality among these patients.

In developed countries, the prevalence of cardiac arrest and CPR among patients admitted in PCICUs have varied between 1.5 and 6% during the last 15 years.⁵⁻⁷ Survival rate of these patients has been 8.8-31% according to general reports.⁵⁻⁷ Survival rates of patients following cardiac arrest and respiratory arrest have been reported as 7% and 33%, respectively.⁷ There is inadequate data about the outcomes of cardiac arrest in patients after cardiac surgery in PCICUs. Moreover, survival markers are not well-identified. However, a previous study suggested long-term use of cardiopulmonary bypass pump (CBP) and high levels of serum lactate after surgery as major markers of cardiac arrest in children.⁸ Another research on patients in PCICUs indicated that cardiac arrest had better outcomes in infants compared to older children. In addition, infants with more severe hemodynamic dysfunction, lower blood pressure, and higher support of high-

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dose inotropic agents had lower survival rates. The present study aimed to identify the outcomes and related factors of cardiac arrest following CPR in pre-school aged children.

Materials and Methods

This descriptive-analytical study was conducted during 2001-02. All children younger than seven years of age who had been admitted in the PCICU of Shahid Rajaie Hospital (Tehran, Iran) after cardiac surgery were evaluated. All cases of cardiac arrest in PCICU were included through census sampling. Patients were divided into survivors (who responded to CPR and regained vital signs particularly palpable spontaneous pulse) and non-survivors (who died after CPR).

Using patient records, cardiac catheterization, vital signs of patients in the PCICU, arterial blood gas test results, disease course, physician's order, and the report of the nurse in charge were extracted. The crude data was recorded in a questionnaire and then analyzed using SPSS for Windows 10.0 (SPSS Inc., Chicago, IL, USA). Various indices (including median, mean, and ratio) and tests (Fisher's exact, Student's t, and chi-square tests) were used to analyze data. P values less than 0.05 were considered statistically significant.

Results

During the one-year period of study, 529 children under seven years old were admitted to the PCICU. Overall, 59 cases (11%) of cardiac arrest were detected and CPR was carried out for them. CPR success rate was 37%. The mean age of survivors and non-survivors was 17.8 and 15.9 months, respectively

(Table 1). While 91.5% of the patients had biventricular physiology, 8.5% had univentricular physiology.

Diagnosis and type of congenital heart disease are summarized in table 2. The most prevalent congenital heart disease was ventricular septal defect (VSD). Cyanotic heart diseases were more common among patients with cardiac arrest. The mean heart rate before the cardiac arrest was 109.0 ± 40.8 beats per minute (bpm) in survivors and 93.0 ± 42.9 bpm in non-survivors. A significant difference was observed in mean arterial blood pressure of survivors and non-survivors (43.8 ± 11.3 vs. 37.8 ± 15.2 mmHg). Therefore, successful CPR was associated with higher mean arterial blood pressure. In addition, CPR success rate in patients with systolic blood pressure lower and greater than 60 mmHg was 31.8% and 68.2%, respectively ($P < 0.05$). On the other hand, CPR was successful in 22.7% of patients with diastolic blood pressure below 30 mmHg and in 77.3% of those with diastolic blood pressure above 30 mmHg ($P = 0.02$).

The mean pH in survivors and non-survivors was 7.20 ± 0.20 and 7.12 ± 0.30 , respectively ($P > 0.05$). There were no significant differences between survivors and non-survivors in mean rate of arterial oxygen saturation ($73.8 \pm 25.1\%$ vs. $66.7 \pm 28.9\%$) or mean bicarbonate concentration (73.8 ± 8.2 vs. 17.2 ± 6.4 mEq/L) (Table 3).

Among 80% of patients with cardiac arrest who had received inotropic agents, 30% had been prescribed with one inotropic agent and 70% had been prescribed with more than one agent. CPR success rates in the mentioned patients were 35.7% and 42.4%, respectively. No significant relationship was seen between increased number of inotropic agents and CPR success rate.

Table 1. Age, weight, duration of cardiopulmonary bypass pump (CBP) and aortic clamping in patients who survived cardiopulmonary resuscitation (survivors) and those who died (non-survivors)

Parameter		Survivors (n = 22)	Non-survivors (n = 37)	P
Age (months)	Mean \pm SD	17.8 \pm 21.1	15.9 \pm 20.6	0.70
	Median (min-max)	6.5 (1.0-60.0)	7 (0.6-72.0)	
Weight (kg)	Mean \pm SD	7.2 \pm 4.2	0.4 \pm 3.5	0.40
	Median (min-max)	5.3 (2.7-16.0)	5.4 (2.7-14.0)	
Duration of CBP use* (min)	Mean \pm SD	93.3 \pm 51.1	79.9 \pm 19.9	0.44
	Median (min-max)	70.0 (15.0-160.0)	83.0 (39.0-110.0)	
Duration of aortic clamping* (min)	Mean \pm SD	55.1 \pm 35.9	37.1 \pm 17.9	0.16
	Median (min-max)	38.0 (4.0-116.0)	40.0 (14.0-72.0)	

* CBP and aortic clamping were used in 11 survivors and 11 non-survivors.

Table 2. Diagnosis and type of congenital heart disease in the study subjects

Diagnosis	N (%)
Ventricular septal defect	10 (16)
Transposition of great arteries	9 (15)
Tetralogy of fallot	8 (13)
Atrioventricular septal defect	10 (6)
Total anomalous pulmonary venous connection	10 (6)
Ventricular septal defect and pulmonary atresia	6 (4)
Tricuspid atresia	6 (4)
Coarctation of aorta	6 (4)
Aortic valve stenosis	5 (3)
Pulmonary atresia	3 (2)
Ventricular septal defect and pulmonary stenosis	3 (2)
Single ventricle	1 (1)

Table 3. Heart rate, mean arterial blood pressure, and laboratory findings for arterial blood gases before cardiac arrest in patients who survived cardiopulmonary resuscitation (survivors) and those who died (non-survivors)

Parameter		Survivors (n = 22)	Non-survivors (n = 37)	P
Heart rate (bpm)	Mean ± SD	109.2 ± 40.8	93.2 ± 12.9	0.08
	Median (min-max)	109.0 (30.0-168.0)	100.0 (23.0-167.0)	
Oxygen partial pressure (mmHg)	Mean ± SD	81.3 ± 97.6	60.4 ± 32.2	0.25
	Median (min-max)	50.0 (12.0-387.0)	54.0 (12.0-138.0)	
Oxygen saturation (%)	Mean ± SD	66.7 ± 28.9	73.8 ± 25.1	0.35
	Median (min-max)	82.0 (18.0-100.0)	67.0 (11.0-99.0)	
Carbon dioxide partial pressure (mmHg)	Mean ± SD	46.6 ± 28.3	53.2 ± 26.6	0.46
	Median (min-max)	40.0 (14.0-152.0)	47.0 (13.0-119.0)	
Bicarbonate concentration (mEq/L)	Mean ± SD	18.4 ± 8.3	17.2 ± 6.4	0.50
	Median (min-max)	17.0 (4.0-39.0)	18.0 (5.0-29.0)	
pH	Mean ± SD	7.20 ± 0.20	7.12 ± 0.30	0.29
	Median (min-max)	7.26 (6.80-7.50)	7.15 (6.00-7.60)	
Mean arterial blood pressure (mmHg)	Mean ± SD	43.8 ± 113.0	37.8 ± 15.2	0.04

Table 4. Parameters related to cardiopulmonary resuscitation (CPR) in survivors and non-survivors

Parameter		Survivors (n = 22)	Non-survivors (n = 37)	P
Period between cardiac arrest and surgery (hours)	Mean ± SD	110.1 ± 188.4	240.2 ± 62.4	0.34
	Median (min-max)	25 (2-840)	31 (1-3600)	
Lowest pH during CPR	Mean ± SD	7.07 ± 0.20	6.99 ± 0.24	0.22
	Median (min-max)	6.99 (6.63-6.79)	6.94 (7.49-6.50)	
CPR duration (min)	Mean ± SD	36.6 ± 22.1	41.5 ± 20.7	0.39
	Median (min-max)	30 (15-120)	30 (20-135)	

CBP was used for 21 patients. The duration of CBP use was less than 90 minutes in 62% of the cases. Maximum duration of CBP use was 150 minutes. The mean duration of CBP use in survivors and non-survivors was 93.9 ± 19.9 and 79 ± 19.9 minutes, respectively ($P > 0.05$) (Table 3). CPR success rate in patients with and without history of cardiac arrest was 67.8% and 10%, respectively ($P < 0.001$). The mean lowest pH during CPR was 7.07 ± 0.20 for survivors and 6.99 ± 0.24 for non-survivors. However, the difference between the two groups was not statistically significant (Table 4).

Discussion

In this study, among 529 children younger than seven years of age in PCICU, 59 cases (11%) of cardiac arrest were observed and CPR success rate was 37%. Previous studies have reported the in-hospital survival rate and long term survival rate after CPR as 13-52% and 5-27%, respectively.^{9,10} In a 15-year long study, Slonim et al. found that 1.5-6% of children admitted to pediatric intensive care unit suffered from cardiac arrest and required CPR.⁵ In a study by Rhodes et al., cardiac arrest and thus the need for CPR was detected in 6% of infants after cardiac surgery.¹¹

The rates of cardiac arrest in our center and other parts of the hospital were not considerably different (11% vs. 13%). However, the rate was higher in our patients compared to those admitted in intensive care unit (ICU).⁹ The difference might have been caused by advanced facilities and greater experience, awareness, and coordination of the staff in ICU.

There was not a significant difference in mean age between survivors and non-survivors in the current study. Similarly, Rhodes et al. suggested that age was not effective on the success of CPR.¹¹

Although CPR success rate was higher in patients with univentricular physiology compared to those with biventricular physiology, there was no significant relationship between the CPR success rate and the physiology of cardiac patients. Likewise, Rhodes et al. reported that univentricular physiology was not an important risk factor for mortality.¹¹ Moreover, mean heart rate and success of CPR were not significantly related since about 83% of survivors and 70% of non-survivors had a heart rate more than 60 bpm. In agreement with our findings, Rhodes et al. indicated that heart rate before cardiac arrest and CPR success rate were not significantly correlated.¹¹

We detected a statistically significant difference in mean arterial blood pressure between survivors and non-survivors. CPR success rate has been previously reported to be positively associated with higher mean arterial blood pressure.¹¹ On the other hand, CPR success rate was significantly higher in patients with systolic blood pressure greater than 60 mmHg and those with diastolic blood pressure greater than 30 mmHg. The reason for this association can be better hemodynamic stability of patients and maintaining blood supply to regain vital signs in vital organs. Rhodes et al. found a similar significant relationship between mean arterial blood pressure and success of CPR.¹¹

In the current study, there were no significant differences in mean pH, oxygen saturation, bicarbonate concentration, or the lowest pH during CPR between survivors and non-survivors. In their study on infants, Rhodes et al. did not find significant correlations between CPR success rate and any of the abovementioned parameters except the lowest pH during CPR.¹¹

We failed to find a significant relationship between increased number of inotropic agents and improved CPR success rate. Rhodes et al. allocated higher scores to increased number of inotropic agents. Similar to our findings, they showed no

significant relationship between CPR success rate and increased number of inotropic agents.¹¹ In addition, in agreement with the findings of Rhodes et al. in infants,¹¹ there was no significant difference in mean duration of CBP use between survivors and non-survivors in the present study.

History of cardiac arrest was significantly related with increased CPR success rate. The possible reason might have been higher attention and support of the staff of PCICU to patients with history of cardiac arrest. They could also regain vital signs due to their hemodynamic status and underlying heart disease. However, this parameter has not been investigated in other studies.

Conclusion

Postoperative cardiac arrest in children is a major concern PCICU. Undesirable CPR outcomes are expected in cases with hemodynamic dysfunction (lower mean arterial blood pressure). Patients with univentricular physiology and/or history of cardiac arrest are not more prone to post-arrest mortality risk.

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Conflict of Interests

Authors have no conflict of interests.

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Autonomic function change following a supervised exercise program in patients with congestive heart failure

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Original Article

Abstract

BACKGROUND: Few studies have investigated changes in autonomic function after training in patients with cardiovascular diseases, particularly patients with congestive heart failure (CHF). Heart rate recovery (HRR) is a strong predictor of mortality in coronary artery disease (CAD) patients. The aim of this study was to determine the effect of 8 weeks of supervised exercise training on autonomic function, which were assessed by heart rate, systolic blood pressure (SBP), and rate-pressure product (RPP) in CHF patients.

METHODS: 65 patients aged 57-82 years with CHF were assigned to two groups randomly. The first group received a supervised 8-week aerobic training program of 30-45 min sessions, 3 days per week on alternate days, while controls received standard medical care and were followed up. Body weight, body mass index, functional capacity, resting heart rate, HRR, resting systolic blood pressure, peak heart rate, peak systolic blood pressure, and RPP were measured before and after the study period. Medications and diet recommendations remained unchanged in both groups during the study period.

RESULTS: The exercise group consisted of 33 patients with mean age of 61.54 ± 5.89 years and the controls were 32 patients with mean age of 60.94 ± 5.03 years. One-way analysis of variance (ANOVA) with repeated measures revealed a statistically significant difference in the exercise group compared to the control group regarding body mass index, resting heart rate, heart rate recover, functional capacity, peak heart rate, peak systolic blood pressure, peak RPP after 8 weeks ($P \leq 0.05$).

CONCLUSION: In conclusion, a multidisciplinary CR program with supervised exercise training support significantly improves functional capacity and autonomic function in CHF patients. Therefore, a supervised and guided exercise training program is safe and beneficial for patients with CHF with different etiologies.

Keywords: Aerobic Exercise, Cardiorespiratory Fitness, Hemodynamics, Autonomic Function, CHF

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Introduction

Cardiovascular diseases, particularly congestive heart failure (CHF), are the most common cause of human deaths in the world.¹ According to WHO estimates, in 2002, 16.7 million people in the world die of cardiovascular diseases each year.² According to previous studies 46% of deaths in Iran each year are from cardiovascular disease.³⁻⁴ Autonomic nervous system dysfunction appears to be involved in the pathophysiology of coronary artery disease and is associated with an increased risk of death.⁵⁻⁷

Autonomic function can be appraised by measuring resting heart rate, heart rate variability, or heart rate recovery (HRR) following exercise.⁶⁻⁷

Physical activity and function capacity improvement is critical in primary and secondary prevention of cardiovascular disease.⁸ Regular aerobic exercise training and cardiac rehabilitation has been shown to reduce the rate of mortality, improve functional capacity, and control the risk factors in myocardial infarction patients.⁹⁻¹²

The term cardiac rehabilitation refers to

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coordinated, multifaceted interventions designed to optimize a cardiac patient's physical, psychological, and social functioning, in addition to stabilizing, slowing, or even reversing the progression of the underlying atherosclerotic processes, thereby reducing morbidity and mortality.¹³⁻¹⁴

Exercise in the outpatient setting is performed under the supervision of health care providers with monitoring based on exercise tolerance test results. Moreover, patients are typically advised to complete a period of supervised aerobic exercise training as adherence to these programs is usually insufficient.¹⁵

The evaluation of the cardiovascular response to various modes of aerobic exercise is critical to the clinician supervising and prescribing exercise programs. Although an acute period of aerobic exercise can cause critical cardiovascular changes, there are few and controversial published data on the effect of different exercise intensities on blood pressure, heart rate, and rate pressure product (RPP), an index of myocardial oxygen consumption, which is calculated by multiplying the heart rate (HR) and the SBP).^{16,17} Other studies have used RPP to estimate changes in myocardial oxygen consumption during physical training of individuals with myocardial infarction disease. Ribeiro et al. observed a significant decrease in resting heart rate, while they found no significant change in systolic and diastolic blood pressure, and rate-pressure product at rest and following exercise sessions in patients after a first acute myocardial infarction.¹⁸ Robinson and Collier et al. found that effort angina pectoris (angina threshold) was reproducible at fixed levels of the RPP.^{19,20} May and Nagle reported that the RPP of patients with coronary artery disease significantly increased during maximal exercise, and decreased significantly during submaximal exercise.²¹ De Backer et al. reported a significant decrease in RPP during each of the three submaximal work loads in the experimental group with anterior myocardial infarctions.²² Kargarfard et al. found an increase in cardiac function and no changes in diastolic indices during 8 weeks of aerobic exercise training in myocardial patients.²³ Due to the importance of cardiac rehabilitation for the performance of many daily activities, we were interested in evaluating the effects of an 8-week aerobic exercise program on BP, HR, and RPP in patients with congestive heart failure (CHF).

Materials and Methods

Subjects

The current study was approved by the Ethics

Committee of Isfahan Cardiovascular Research institute (ICRI, a WHO collaborating center) and the University of Isfahan, before the study was launched.

Male and female patients who were referred to ICRI with a history of myocardial infarction and a diagnosis of CHF between June 2010 and December 2011 were invited to take part in this study.

The inclusion criteria were: being residents of Isfahan; aged over 50 years; currently not taking part in regular physical activities; having heart failure for at least three months; having a left ventricular ejection fraction of $\leq 35\%$ on echocardiogram and have been in functional class (FC) II according to the New York Heart Association (NYHA) in the previous 2 years. Patients should be referred by a cardiologist. The exclusion criteria included NYHA FC, acute myocardial infarction, or revascularization within the past 4 months, hypotension, unstable angina, ventricular or symptomatic arrhythmias, obstructive aortic valve disease, chronic obstructive pulmonary disease, hypertrophic obstructive cardiomyopathy, severe musculoskeletal problems preventing exercise, and case-note reported dementia or current severe psychiatric disorder.

Sixty-five male and female patients with CHF agreed to participate in the study. They were assigned randomly to two groups of exercise ($n = 33$) and control ($n = 32$). Participants signed a written informed consent after being informed of the details of the study.

There was no alteration in the prescribed medications and diet in both groups throughout the study. All subjects underwent comprehensive medical screening prior to participation, including medical history, physical examination, and stress testing. The patients did not participate in an exercise program for at least 3 months prior to the study; they were instructed to avoid any extra exercise not included in the study training program.

Experimental design

All patients followed a familiarization training period of 2 weeks. Thereafter, each patient underwent anthropometric evaluation, physiological evaluation, and exercise stress testing using the Naughton protocol. Afterwards, they participated in a supervised and systematic exercise program of aerobic training three times per week for 8 weeks. The training program was arranged to provide an alternative day for the replacement of a possible lost session during the week. The baseline assessment was repeated after 8 weeks of training.

Aerobic training program

Aerobic exercise consisted of walking/jogging on

the treadmill three times per week. Each session lasted about 45-60 min including a warm-up period (5-10 min), stretching exercises (10 min), the main program with treadmill exercise (15-30 min), and a cool-down period (15 min including stretching). During the first 4 weeks, the intensity of aerobic exercise was 60-70% of maximum heart rate (HR_{max}) achieved during stress testing. Thereafter, training intensity was increased to 70-80% HR_{max} according to the individual adaptation observed during training sessions.

Testing procedures

Demographic measures and medical history

A detailed medical history was obtained from each participant. The medical history addressed all of the aforementioned exclusion criteria, as well as history of hyperlipidemia, dyspnea, diabetes hypertension or other symptoms of CHF.

Height was measured using a stadiometer, with the measurement taken to the nearest 0.1 cm. Weight was measured using a balance scale, with the measurement taken to the nearest 0.1 kg. Height and weight measurements were then used to calculate body mass index (BMI); BMI = (weight in kilograms)/(height in meters²). Waist-to-hip ratio was measured with a measuring tape, with a horizontal measure at both the waist and hip sites, taken to the nearest 0.1 cm. Blood pressure and heart rate were measured with a sphygmomanometer following 30 minutes of rest.

Exercise stress testing

All patients underwent a symptom-limited exercise test on the treadmill with electrocardiogram (ECG) monitoring according to the modified Naughton protocol. The Naughton protocol is a submaximal study which is used for high-risk patients. It uses 10 3-min exercise periods. The modified Naughton protocol has 2-min stages and starts at a lower metabolic equivalent (MET) workload increasing by patients stop because of either fatigue or dyspnea. It contains a 4-min warm-up and a set speed of 2.0 miles per hour (mph). The grade increases 3.5% every 2 min until maximum effort is achieved. This approach allows for a better tolerated gradual progression in exercise. Moreover, it is a more accurate assessment of functional capacity. During aerobic exercise sessions in these patients, exertion levels are often evaluated by the Borg Rating of Perceived Exertion Scale, because the rate of perceived exertion and heart rate (HR) are linearly concerned with each other and work intensity.^{24,25}

Resting HR and peak HR were measured using a 12-lead electrocardiograph with an automatic

ST-segment analysis, while blood pressure was recorded manually at rest and then at 3-min intervals during the stress test.

Peak HR was considered the highest mean 10-s value achieved during the test. Blood pressure was measured with a mercury sphygmomanometer at rest, during the last 15 seconds of exercise near the end of the test. Peak systolic and diastolic blood pressures were recorded as the highest value achieved during the test. PRR product was computed by multiplying peak HR by peak systolic blood pressure. HRR was determined by calculating the difference between HR at peak exercise and HR 1 min after completion of exercise.¹⁰ Patients were instructed to sit after ending the test, and there was no cool-down period until after HRR was recorded.¹¹ There was then a 4-min cool-down period that consisted of light walking at 2 km/h on a flat treadmill (0% grade).

Statistical analysis

All data are expressed as means \pm SD. Student's t-test was used to compare the baseline characteristics of exercise and control groups. Paired t-tests were performed on continuous variables to determine differences in cardiorespiratory fitness and hemodynamic measurements in the exercise and control groups. Finally, one-way ANOVA with repeated measures was performed on cardiorespiratory fitness and hemodynamic variables to determine differences between the two groups after 8 weeks. SPSS for Windows (version 18; SPSS Inc., Chicago, IL., USA) was used to analyze all data. Statistical significance was assumed for P values < 0.05.

Results

A total of 70 eligible patients with CHF were recruited from June 2010 to December 2011, but only 65 (33 exercise and 32 controls) patients completed the study within 8 weeks. Five of the 70 patients, 2 in the exercise group and 3 in the control group, were not able to complete the study for non-medical reasons and were not included in the data analysis.

Table 1 lists the baseline data (mean \pm SD) for age, height, body weight, body mass index, resting heart rate, heart rate recovery, resting diastolic blood pressure, resting systolic blood pressure, peak functional capacity, peak heart rate, and peak rate pressure product between cases and controls.

The patients had a mean age of 61.25 ± 5.45 years, mean height of 167.12 ± 7.94 cm, mean weight of 73.06 ± 7.80 kg, and mean BMI of 26.11 ± 1.45 kg/m². There were no significant

differences in all characteristics of the cardiorespiratory fitness and hemodynamics between exercise and control groups at baseline ($P > 0.05$; Table 1).

At the initial exercise stress testing, before physical rehabilitation, there was no significant difference between groups in regard to functional capacity; which were 5.11 ± 0.93 METs in exercise group and 5.19 ± 0.83 METs in control group.

Physical training was prescribed on the basis of initial exercise capacity and exercise tolerance, and the first part of rehabilitation was performed as a physical rehabilitation. At the end of the rehabilitation phase, the functional capacity was

assessed again by the same exercise stress protocol as the initial one.

Table 2 lists the mean \pm SD values for all of cardiorespiratory fitness and hemodynamics parameters for each group before and after the 8-week study. It also shows the differences in all outcomes included in the study from the baseline to eight weeks, within and between the exercise and control groups. Patients in the exercise group have shown statistically significant improvement in resting heart rate, heart rate recovery, resting systolic blood pressure, peak functional capacity, peak heart rate, and peak RPP except for the body weight, body mass index and resting diastolic blood pressure.

Table 1. Baseline characteristics of cardiorespiratory fitness and hemodynamics in heart failure patients before the study

Characteristics	Exercise training group (n = 33)	Control group (n = 32)	P
Age (year)	61.54 \pm 5.89	60.94 \pm 5.03	0.66
Gender (male: female)	22: 11	17: 15	> 0.05
Weight (kg)	73.54 \pm 7.54	72.56 \pm 8.16	0.62
Height (cm)	168.30 \pm 7.94	165.91 \pm 7.88	0.23
BMI (kg/h ²)	25.93 \pm 1.44	26.30 \pm 1.46	0.32
FC (METs)	5.11 \pm 0.93	5.19 \pm 0.83	0.70
RHR (beats/min)	87.03 \pm 4.50	86.19 \pm 3.75	0.42
RSBP (mmHg)	151.50 \pm 6.51	148.41 \pm 6.79	0.18
RDBP (mmHg)	85.06 \pm 11.96	90.06 \pm 9.92	0.07
Peak HR (beats/min)	130.01 \pm 4.05	130.46 \pm 3.13	0.61
HRR (beats/min)	21.13 \pm 4.44	20.66 \pm 4.93	0.69
Peak SBP (mmHg)	162.45 \pm 5.93	159.34 \pm 6.53	0.18
Peak DBP (mmHg)	99.52 \pm 5.85	98.31 \pm 5.81	0.41
Peak RPP (mmHg \times bpm)	21117.54 \pm 958.89	20789.98 \pm 1013.88	0.19

Note: BMI: body mass index; RHR: resting heart rate; HRR: heart rate recovery; RDBP: resting diastolic blood pressure; RSBP: resting systolic blood pressure; Peak FC: Peak Functional Capacity; Peak HR: Peak heart rate; Peak RPP: Peak rate pressure product; derived from independent Student t-tests

Table 2. Comparison of cardiorespiratory fitness and hemodynamics of exercise and control group patients before and after the study

Characteristics	Exercise (n = 33)			Control (n = 32)			P**
	Before	After	P*	Before	After	P*	
Weight (kg)	73.54 \pm 7.54	73.14 \pm 7.32	0.12	72.56 \pm 8.16	73.98 \pm 8.64	0.02	0.97
BMI (kg/h ²)	25.93 \pm 1.44	25.79 \pm 1.41	0.14	26.30 \pm 1.46	26.86 \pm 1.44	0.01	0.04
EF (%)	32.30 \pm 3.87	37.94 \pm 5.33	0.000	31.44 \pm 3.61	30.62 \pm 3.22	0.11	0.000
FC (METs)	5.11 \pm 0.93	6.44 \pm 1.22	0.000	5.19 \pm 0.83	4.85 \pm 0.84	0.02	0.001
RHR (beats/min)	87.03 \pm 4.50	83.33 \pm 5.04	0.000	86.19 \pm 3.75	88.22 \pm 4.67	0.05	0.03
RSBP (mmHg)	152.45 \pm 5.93	150.24 \pm 6.35	0.02	149.34 \pm 6.53	149.03 \pm 7.83	0.82	0.14
RDBP (mmHg)	85.06 \pm 11.96	83.54 \pm 10.44	0.10	90.06 \pm 9.92	90.97 \pm 10.15	0.22	0.02
Peak HR (beats/min)	130.01 \pm 4.05	141.64 \pm 4.61	0.000	130.46 \pm 3.13	132.99 \pm 4.35	0.01	0.000
HRR (beats/min)	21.13 \pm 4.44	25.97 \pm 6.34	0.000	20.66 \pm 4.93	19.62 \pm 4.27	0.02	0.003
Peak SBP (mmHg)	162.45 \pm 5.93	173.00 \pm 7.81	0.000	159.34 \pm 6.53	162.03 \pm 7.83	0.06	0.000
Peak DBP (mmHg)	99.52 \pm 5.85	97.70 \pm 4.87	0.003	98.31 \pm 5.81	99.78 \pm 6.08	0.03	0.74
Peak RPP (mmHg \times bpm)	21117.54 \pm 958.89	24513.64 \pm 1527.60	0.001	20790.98 \pm 1013.88	21553.12 \pm 1333.38	0.005	0.000

Note: BMI: body mass index; EF: ejection fraction; RHR: resting heart rate; HRR: heart rate recovery; RDBP: resting diastolic blood pressure; RSBP: resting systolic blood pressure; FC: functional capacity; Peak HR: Peak heart rate; Peak SBP: peak systolic blood pressure; Peak DBP: peak diastolic blood pressure; Peak RPP: Peak rate pressure product; * significant difference between before and after the intervention in each group; ** significant difference between exercise and control groups at the 8th week

Functional capacity and ejection fraction were increased in the exercise group from 5.11 ± 0.93 METs to 6.44 ± 1.22 METs, and 32.30 ± 3.87 to 37.94 ± 5.33 , respectively ($P < 0.001$). However, they were decreased in the control group ($P < 0.001$).

At the end of the rehabilitation phase, at the same sub maximal exercise level, the resting HR and resting SBP were significantly reduced in the exercise group ($P < 0.01$), when compared with pre-training values (Table 2). Moreover, the resting HR increased significantly in the control group ($P < 0.05$).

One-way analysis of variances (ANOVA) with repeated measures revealed a statistically significant difference in the exercise group compared with control group in their body mass index, resting heart rate, heart rate recovery, functional capacity, peak heart rate, peak systolic blood pressure, and peak rate pressure product ($P \leq 0.05$; Table 2).

Discussion

Most interventional studies evaluated the efficacy of aerobic exercise in lowering BP and HR. Information regarding the efficacy of aerobic exercise training on autonomic function factors is limited.

The present study aimed to evaluate the effects of 8 weeks aerobic exercise training on RPP, maximal and rest heart rates, and blood pressure in patients with CHF. To define the effect of exercise training per se, other important variables were controlled such as medications use and diet. The main finding of our investigation is that cardiac rehabilitation independently improves cardiac autonomic function.

In this study, we found that an 8 week aerobic exercise program improved resting heart rate, heart rate recovery, resting systolic blood pressure, peak functional capacity, peak heart rate, and RPP significantly ($P < 0.05$). While the body weight, body mass index, and resting diastolic blood pressure in the exercise group did not show any significant changes. At the end of the rehabilitation, exercise capacity and ejection fraction were increased significantly in the exercise group, while they were decreased in the control group ($P < 0.001$).

At the end of the rehabilitation phase, at the same sub maximal exercise level, the resting HR and resting SBP were significantly reduced in the exercise group ($P < 0.01$), when compared with pre-training values (Table 2). However, there was a

significant increase in the resting HR in the control group ($P < 0.05$).

Furthermore, in comparison with baseline data, the exercise group showed significantly higher scores in functional capacity, heart rate recovery, peak heart rate, peak systolic blood pressure, peak diastolic blood pressure, and peak RPP following the 8-week exercise-training program.

One-way analysis of variances (ANOVA) with repeated measures revealed a statistically significant difference between the exercise group and the control group in body mass index, resting heart rate, heart rate recovery, functional capacity, peak heart rate, peak systolic blood pressure, and peak rate pressure product ($P \leq 0.05$).

Previous studies have reported that autonomic nervous system dysfunction appears to be involved in the pathophysiology of coronary artery disease and is associated with an increased risk of death.⁵⁻⁷ Autonomic function can be appraised by measuring resting heart rate, heart rate variability, or heart rate recovery (HRR) following exercise.⁶⁻⁷ Thus, the positive effect of cardiac rehabilitation on cardiac autonomic nervous system is important. Following the rehabilitation program in the present study, all factors in the training group had a significant improvement.

These positive effects on the autonomic nervous system suggested that the results of the current study are supported by decreasing RPP, maximal and resting heart rates, and blood pressure (systolic, mean, and diastolic) observed in the exercise-training group.

In healthy subjects and athletes, heart rate rapidly decreased after exercise. However, during exercise due to the withdrawal of parasympathetic tone and increased sympathetic tone, heart rate increases. Immediately after exercise, heart rate decreases due to rapid reactivation of the parasympathetic nervous system. The ability of the heart rate to recover after exercise is related to the capacity of the cardiovascular system to inverse the autonomic nervous system and baroreceptors adaptation, which is often called vagal reactivation.²⁶

A study by Wu TY et al. (2007) showed that both systolic and diastolic blood pressures at rest and after 8 weeks of exercise were significantly decreased in the training group. However, changes in blood pressure were not significantly different between the training and control groups. This may be due to the relatively low number of patients ($n = 18$ per group) to achieve statistical significance.²⁷

Another study performed by Ribeiro et al. showed that resting heart rate decreased by 5 beats per minute in the exercise group. However, there was no change observed in systolic and diastolic blood pressures, and RPP at rest and peak; this finding is inconsistent with the results of this research.¹⁸ The results of the present study is consistent with Forjaz et al., May and Nagle and MacMasters et al.^{16,21,28}

Adams et al. showed that the mean RPP during clinical training sessions on the treadmill was far below the clinically safe rate for the training group.²⁹ In the study by Kim et al., no significant differences were observed in both groups after a 6-week rehabilitation program regarding rest and peak systolic and diastolic blood pressures, resting heart rate, and maximal pressure produced. However, maximum heart rate and submaximal RPP were significantly different.³⁰ Ahn et al. reported that in comparison to the exercise group, there was no significant difference in the RPP of the control group. Such significant progression can be credited to cardiac rehabilitation by improving exercise tolerance and exercise duration, as well as increasing heart rate and systolic blood pressure.³¹ The Asian Department of Cardiovascular Prevention and Rehabilitation (2011) reported that aerobic exercise has a moderate effect on resting heart rate, caused no changes in systolic and diastolic blood pressure, and has a strong effect on submaximal RPP.³² However, the results of this study support previously mentioned studies.

In conclusion, a multidisciplinary CR program with supervised exercise training support significantly improves functional capacity and hemodynamics parameters in CHF patients. Therefore, a supervised and guided exercise training program is safe and beneficial for patients with CHF with different etiologies.

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Conflict of Interests

Authors have no conflict of interests.

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Diagnostic performance of 64-row coronary CT angiography in detecting significant stenosis as compared with conventional invasive coronary angiography

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Original Article

Abstract

BACKGROUND: The aim of the present study is to evaluate the accuracy of 64-multidetector-row computed tomography angiography (CTA) in comparison to conventional invasive angiography (CIA) in the diagnosis of significant stenosis ($\geq 50\%$) of coronary artery tree.

METHODS: Assessment of CTA in the detection of coronary artery disease (CAD) was performed in patients referred because of symptoms or stress studies suggestive of ischemia. For this purpose, among more than 1000 cases of coronary CTA in a 20 months period a study population of 54 patients suspected to have significant stenosis of the coronary artery tree was investigated. The CIA procedure was performed in these patients one month after CTA. The accuracy of CTA in detecting significant stenosis was compared to CIA.

RESULTS: For vessel based analysis of 179 coronary vessels, CTA had a sensitivity of 96%, specificity of 87.5%, positive predictive value of 90.5%, and negative predictive value of 94.6%. For patient-base analysis, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CTA were 97.9%, 28.6%, 66.6%, and 90.2%, respectively.

CONCLUSION: The findings of this study reveal that CT angiography with 64-slice scanner could be considered as a suitable technique for rapid triage of patients presenting to hospitals with chest pain. High values of sensitivity and PPV reveal the good performance of CTA in detecting CAD.

Keywords: Coronary Artery Disease (CAD), Computed Tomography Angiography (CTA), Conventional Invasive Angiography (CIA)

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Introduction

Coronary artery disease (CAD) is one of the main causes of disability and death all over the world. For several decades, conventional invasive angiography (CIA) has been considered as the well-established gold standard for making the diagnosis of CAD. Conventional invasive angiography (CIA) is highly reliable compared to other indirect evaluation methods such as stress testing. CIA has a high diagnostic ability to determine the extent, location, and severity of coronary obstructive lesions. Thus, this method remains the main standard for the diagnosis of CADs. However, CIA is not a good choice in some cases due to its invasive nature and

the risk of complications, i.e. arrhythmia, myocardial infarction, stroke, access site problems, etc. Finally, nearly one third of CIAs were reported to be normal, and therefore this invasive procedure is not necessary for all patients.¹ Furthermore, there are constraints on the number of CIA that can be undertaken, in terms of the cardiologist's time.² Therefore, an accurate non-invasive alternative evaluation method for diagnosing CAD is highly desirable. Note that noninvasive modalities, like stress echocardiography and myocardial radionuclide scan, are unable to evaluate the coronary artery since these methods evaluate only the corresponding myocardial segment. In order to overcome

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the complications of CIA, multi-slice computed tomography angiography (CTA) has been proposed in recent years as an alternative procedure for determining the presence of coronary obstructions. With the recent development in hardware with multiple detectors, the spatial and temporal resolutions of images have been significantly improved and consequently CTA has become the center of interest for clinicians. The 4-slice, 16-slice, and 64-slice imaging machines have been utilized in 1998, 2001, and 2004, respectively.² These machines facilitated the rapid identification and assessment of atherosclerosis within the moving coronary arteries and potentially reduced the necessity for CIA. Abdulla et al. evaluated the diagnostic accuracy of 64-slice CTA compared with the standard reference CAD.³ Based on their systematic search, 27 studies including 1740 patients were considered for meta-analyses. Their review paper validated CTA as a potential alternative to CIA in patients suspected of having coronary stenosis. Mowatt et al. undertook another comprehensive systematic review and meta-analysis of the clinical effectiveness and cost-effectiveness of 64-slice or higher CTA as an alternative to CIA for detecting CAD. The diagnostic accuracy and prognostic studies enrolled over 2500 and 1700 people, respectively.⁴ Other systematic reviews have also been conducted on evaluation of 64-slice CTA in the diagnosis and assessment of coronary artery disease.^{2,5,6} Stein et al. performed a systematic review on 64-slice CTA for diagnosis of CAD.⁷ They concluded that negative CTA reliably excluded significant CAD. However, the data suggest that stenoses shown on CTA need confirmation. Combining the results of 64-slice CTA with a pretest clinical probability assessment would strengthen the diagnosis.⁷ Further useful findings can be found in other works that have examined the accuracy of CTA in comparison with CIA for detecting CADs.⁸⁻²⁰ The current investigation was conducted using a 64-row-detector CT scanner to evaluate the sensitivity, specificity, negative predictive value, and positive predictive value of CTA in identifying significant stenosis ($\geq 50\%$). The accuracy of 64-row CTA is compared with that of the CIA method as the gold standard.

Materials and Methods

Patients

The study population was chosen from the 1000 patients who were suspected of having coronary artery disease and who referred to the Heart Center

of Al Zahra Hospital between March 2010 and January 2012.

In this study 54 patients asked to participate. According to the cardiologist all these patients underwent CIA one month after CTA was performed. Exclusion criteria for CTA were based on technical factors that made the patient unsuitable for the procedure. These included known allergic reaction to iodinated contrast agents, high baseline heart rate (> 70 beats/min) with contraindication to beta-blockade, atrial fibrillation, inability to hold the breath for 15-s, inability to lie flat, abnormal renal function (serum creatinine level > 1.5 mg/dL). The detailed characteristics of the study population are listed in table 1. The study was approved by the local ethical review board.

Table 1. Patient demographics and clinical indications (n = 54)

	Number	Percentage
Male	34	63
Mean age (years)	59	-
Diabetes mellitus	13	24
Hypertension	22	41
Smoking	15	28
Hyperlipidemia	21	39

Preparation procedure

The patients' heart rates were assessed 1 hour before scanning. Patients with a prescan heart rate of higher than 60 beats/min received 50–100 mg oral metoprolol 1 hour before CTA. In the case of patients with anxiety, 0.5 mg alprazolam was given. If the heart rate was still higher than 60 beats/min at the time of the examination, intravenous propranolol (< 10 mg) was used to achieve a target prescan heart rate of less than 60 beats/min. Sublingual nitrates were used before the procedure.

Scanning Protocol

All patients were scanned with a 64-slice single-source CT scanner (Medical health care GE Work Station RDW 4.3, GE, USA). The scanning parameters applied have been reported in table 2. After calcium scanning, a bolus of 80-100 ml nonionic iodinated contrast medium (Ultravist-300) followed by 50–60 ml of normal saline was injected through an antecubital vein by way of an 18-gauge catheter using a dual injector at a flow rate of 4–6 ml/s. A dose of 15 ml contrast material was used during the bolus timing scan calculated (by the apparatus software) at the level of the descending

aorta. Seven seconds were added to the calculated time to carry out the CT procedure. All data sets acquired were reconstructed from the axial, coronal, and sagittal images using a retrospective electrocardiogram gating with the GE Advantage Windows Workstation 4.3. The data set was reconstructed at 75% of R-R intervals. In cases that motion artifacts resulted in low image quality, additional data sets were reconstructed between 25% and 85% of R-R interval to obtain optimal image quality.

Table 2. Angiographic Scan Parameters

Number of Slices per rotation	64 × 1
Individual detector width	0.625 mm
Rotation time	0.33 sec
Tube voltage	120 kVp
Tube current	320 mA

CTA Image Evaluation

The reconstructed images were visually evaluated for estimation of coronary artery narrowing. Axial images, postprocessing volume-rendered 3D images, the maximum intensity projections, multiplanar reconstructions, and linear conformation of the vessels were used to evaluate vessel stenosis. A significant lesion was defined as more than 50% reduction in lumen diameter. The judgment about the absence/presence of CAD was made after viewing the various images and checking stenosis of main coronary vessels, i.e. left main artery, left anterior descending, circumflex artery, first diagonal, second diagonal, obtuse marginal, right coronary artery and the posterior descending artery.

CIA procedure and analysis

Routine CIA procedure was performed via the femoral or radial artery. All evaluated vessels were classified as normal vessels, having non-significant disease (luminal irregularities resulting in narrowing < 50%), or as having significant stenosis (luminal narrowing ≥ 50%). Accordingly, patients were classified as positive for the presence of significant CAD if there was a significant stenosis in any artery. Comparisons were then made between CTA and

CIA findings.

Statistical Analysis

The CTA accuracy for detecting vessel stenosis was evaluated by four indicative statistical parameters including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). These parameters were calculated for vessels and for the patients and presented as percentages [95% confidence interval]. The sensitivity parameter shows that there is positive CTA among patients with positive CIA. The sensitivity is mathematically determined as the sum of true positive divided by the sum of diseased. The specificity parameter implies the negative CTA among patients with negative CIA. The specificity is calculated as the sum of true negative divided by the sum of non diseased.

Results

Patient-Based Analysis

The characteristics of the 54 patients were analyzed and the results are presented in table 3. The obtained results reveal that 2 patients were diagnosed as normal by both CIA and CTA (true negative). Only 1 patient was considered as normal based on CTA findings, but this patient was diagnosed as abnormal by CIA. This reveals that 1 case was reported as false negative. Figure 1 depicts the typical example of false negative cases where CTA reveals normal coronary arteries but CIA shows obstructive CAD. Of the remaining 51 subjects diagnosed as abnormal on CTA, 46 were confirmed by CIA (true positive). Figure 2 depicts a typical example of true positive cases where both CTA and CIA reveal CAD. Finally, 5 cases were reported abnormal on CTA while proved to be normal by CIA (false positive).

Vessel-Based Analysis

The obtained results of the vessel-based analysis have been reported in table 4. For this analysis 179 vessels were evaluated using both CTA and CIA procedures. According to the vessel-based obtained data presented in table 4, 95 true positive, 70 true negative, 10 false positive, and 4 false negative cases were reported in this study when compared to CIA procedure.

Table 3. Diagnostic performance of CTA for the detection of > 50% stenosis for patient-based analysis

Analysis	N	TP	TN	FP	FN	Sensitivity %	Specificity %	PPV %	NPV %
Patient-based	54	46	2	5	1	97.9	28.6	90.2	66.6

TP: True positive; TN: True negative; FP: False positive; FN: False negative; PPV: positive predictive value; NPV: negative predictive value

Table 4. Diagnostic performance of CTA for the detection of > 50% stenosis for vessel-based analysis

Analysis	N	TP	TN	FP	FN	Sensitivity %	Specificity %	PPV	NPV
Vessel-based	179	95	70	10	4	96	87.5	90.5	94.6

TP: True positive; TN: True negative; FP: False positive; FN: False negative; PPV: positive predictive value; NPV: negative predictive value



Figure 1. A typical example of false negative cases where (a) computed tomography angiography (CTA) reveals no significant stenosis while (b) conventional invasive angiography (CIA) shows a significant stenosis at proximal part of right coronary artery

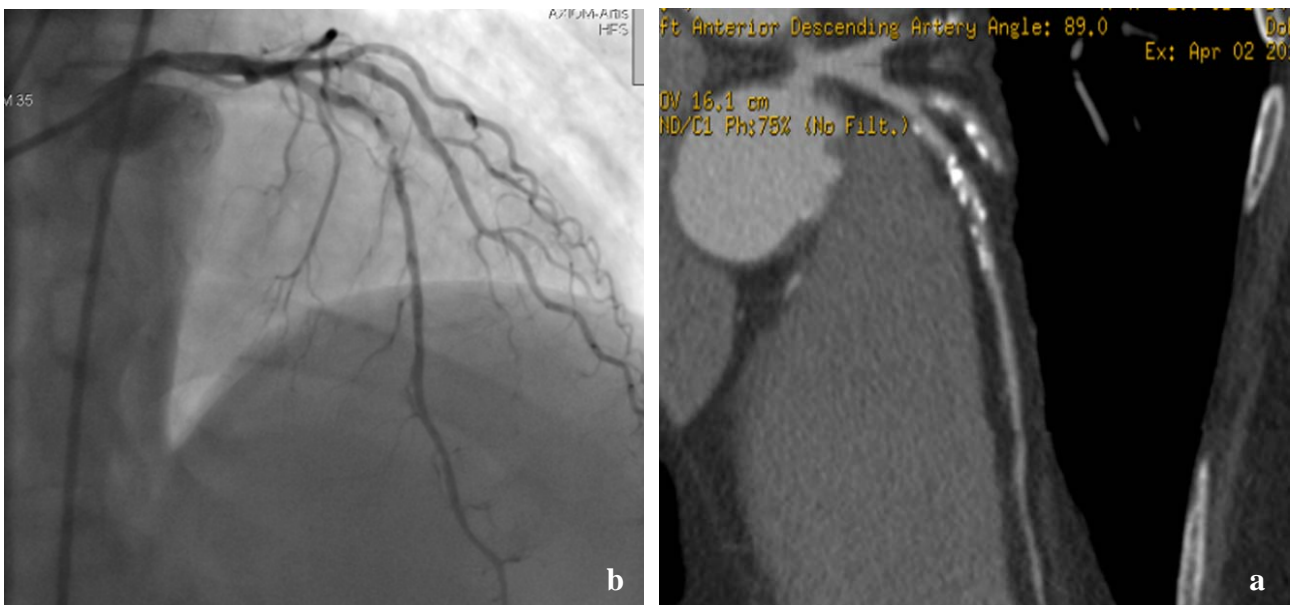


Figure 2. A typical example of true positive cases where both computed tomography angiography (CTA) (a) and conventional invasive angiography (CIA) (b) show a significant stenosis

Discussion

Many progresses have been accomplished to provide time-saving accurate diagnostic protocols for CAD suspected patients. The advent of 64-slice

CT scanners accelerated this evolution. CTA is recommended as useful especially for patients with higher complications of CIA. However, a crucial issue is to understand how close the CTA and CIA

findings are. According to the patient-based data presented in table 3, CTA has a sensitivity of 97.9%, a specificity of 28.6%, a positive predictive value of 90.2%, and a negative predictive value of 66.6% when compared to CIA procedure. Furthermore, a sensitivity of 96%, a specificity of 87.5%, a positive predictive value of 90.5%, and a negative predictive value of 94.6% is reported for vessel-based analysis. Comparison between the obtained results and those presented in other review papers show that both patient-based and vessel-based sensitivity of the present study are very close to the values reported by previous researchers for 64-slice CTA.^{5,6} The high sensitivity of CTA reveals the reliability of this method as a conservative approach for ruling out CAD via a negative CTA result. Note that due to the high sensitivity of CTA it is very improbable to miss any positive case via this method. A similar trend is observed for the PPV parameter. Comparing the present study with other investigations reveals that the computed PPV (90.2% for patient-based and 90.5% for vessel-based analysis) is close to those reported in previous literature.^{5,6} This reveals the good performance of CTA in detecting CAD, and one can conclude that a positive CTA result indicates a significant CAD. In this study, the low values of patient-based specificity and NPV might be attributed to the conservative selection of the study population. Note that CTA was conducted on patients suspected to have a significant CAD instead of randomly selected patients. This conservative approach results in a selection bias and the consequent reduction of the real negative cases, specificity. However, this difference is not observed in the case of vessel-based analysis in which the computed parameters are close to those reported in previous literature.^{5,9,18,19} Interestingly, most (70%) false reports, i.e. false positive and false negative cases, are reported for left anterior descending (LAD) artery. This finding is in accordance with the findings of Sheikh et al., who reported lower sensitivity for LAD vessel in comparison with those of other main vascular tree vessels (RCA and Cx artery).⁹ Moreover, CTA can reliably detect patients who need revascularization (interventionally or surgically) based on the involved vessels and segments. This is important from the clinical point of view.¹¹

Technological advancements

It is expected that the new generation of scanning machines with higher number of slice per rotation (rows) and higher temporal resolution can diminish the inaccuracies of the present 64-slice CT scanners.

Previous research on different generation of multi-detector CT machines (4-slice, 16-slice, and 64-slice scanners) revealed that increase in number of slice per rotation results in more accurate results.²¹ This trend is expected to be continued for the forthcoming multisection scanners with higher number of detectors. For example, new generated 320-row scanners improved image acquisition as well as reduced radiation dose compared with retrospectively gated 64-row CTA.¹⁵ Moreover, in recent years, several modified techniques, i.e. dose modulation, eliminating helical oversampling, prospectively gated approach with electrocardiogram triggering, and etc., have been developed to decrease CTA radiation dose.²²⁻²⁴ These technological advances show that the reliability of CTA can reach that of CIA in the future. Furthermore, a systematic heart rate control might significantly improve the diagnostic accuracy of the present single-source CTA. Note that a comparison between single-source and dual-source CTA revealed the significant influence of heart rate control on enhancing the diagnostic accuracy of single-source 192 CTA.⁸

Limitations

It should be remarked that the present study was preformed based on single-center data, hence the obtained results might not be generalized. The following limitations to the present study should be considered. First, patients were exposed to a higher dose of radiation in CTA procedure in comparison with CIA.¹² Therefore, concerns should be raised about applying conservative radiation dose, and careful patient selection especially in the cases of young people and women of childbearing age.²⁵ Moreover, note that CTA was conducted on patients suspected to have a significant CAD referred for CIA. This, results in a selection bias in the study. Therefore, the present diagnostic performance may not be directly applicable to patients with a lower prevalence of CAD. Finally, it should be noted that heavy coronary calcification and the consequent beam hardening are the major limitations to reliable evaluation of all coronary arteries.²⁶⁻²⁸ In these cases CIA might be more useful than CTA in obtain completely reliable diagnoses. It should be noted that while a calcium score of higher than 600 is known as a limiting parameter for CTA, this was not a dominant limitation in present study. Some technical tricks like higher flow rates of contrast injection, lower heart rates, and reconstruction with sharper kernels and wider window level improved the image quality.²⁹

Future directions

For increasing the diagnostic performance of CTA, one might evaluate the myocardial perfusion. This can be preformed by combining the anatomic data with physiologic significance of the atherosclerotic lesions. Further investigation is required to develop appropriate acquisition protocols for optimal image acquisition and decreased radiation dose. With the developments in CTA technology, future studies should be conducted on reducing radiation exposure, while maintaining high image quality.

Conclusion

The present study may have applied clinical implications for the detection of stenosis of higher than 50%. Results demonstrated moderately good diagnostic accuracy for the assessment of obstructive CAD using 64-row CTA. For vessel based analysis, CTA had the sensitivity, specificity, positive predictive value, and NPV of 96%, 87.5%, 90.5%, and 94.6%, respectively. For patient-based analysis, these values were 97.9%, 28.6%, 66.6%, and 90.2%, respectively. The high value of sensitivity reveals the good performance of CTA in ruling -out CAD. Similarly, it has been reported that high PPV indicates the reliability of CTA in diagnosing CAD. While the mean specificity and NPV of patient-based analysis is lower than those reported in previous literature, this difference is not observed in vessel-based analysis. The findings reveal that CT angiography with 64-slice scanner could be considered as a suitable technique for rapid triage of patients presenting to hospital with chest pains. It should be noted that further investigation is required to determine whether 64-row scanning technology has sufficient resolution to delineate CAD.

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Conflict of Interests

Authors have no conflict of interests.

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Percutaneous coronary intervention of an obstructive left anterior descending artery with anomalous origin of right coronary artery

Laxman Dubey⁽¹⁾

Case Report

Abstract

Coronary artery anomalies are a rare type of congenital anomalies with an incidence of 1.3% during routine cardiac catheterization. Anomalous origin of the coronary arteries is considered an incidental finding without clinical significance. This case describes a patient in whom evaluation of chest pain revealed an obstructive left anterior descending artery as well as an anomalous right coronary artery arising from the left coronary sinus. The patient underwent successful percutaneous coronary intervention of the left anterior descending artery and was discharged home free of angina 3 days later.

Keywords: Anomalous Right Coronary Artery, Obstructive Left Anterior Descending Artery, Percutaneous Coronary Intervention

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Introduction

The incidence of coronary anomalies was found to be 1.3% in a large series of patients undergoing coronary angiography.¹ Of these, most were abnormalities of the origin of the coronary arteries, and a few were coronary artery fistulas. Anomalous origin of the coronary arteries is considered an incidental finding without clinical significance; however, these abnormalities may be responsible for angina pectoris, heart failure and increased risk of sudden death. This case describes a patient in whom evaluation of chest pain revealed an obstructive left anterior descending artery as well as an anomalous right coronary artery arising from the left coronary sinus. The patient underwent successful percutaneous coronary intervention of the left anterior descending artery.

Case Report

A 52-year-old female presented to our center with exertional chest pain for the previous 7 days which had increased in intensity for 1 day. Pain was associated with sweating. She had a history of systemic hypertension but was not on medication. Her electrocardiogram showed sinus rhythm with non-specific T-wave abnormalities. Clinical examination revealed a moderately built female with a blood pressure of 140/80mmHg and a regular pulse at 78 beats per minute. Hemoglobin, white

cell count, differential white cell count, serum electrolytes, renal function tests, and liver function tests were within normal limits. CK-MB was 28U/L and troponin I was negative. Transthoracic echo showed grade 1 left ventricular (LV) diastolic dysfunction, normal LV systolic function, and no wall motion abnormalities. Cardiac catheterization was done via right radial artery approach. Selective catheterization of the left coronary artery (LCA) showed normal left main (LM) coronary artery, normal left circumflex artery (LCX) coronary artery, and a significant obstructive lesion (80%) in mid part of the left anterior descending artery (LAD) just after the first diagonal branch, with good distal flow (Figure 1).

During selective catheterization of the LCA, filling in the right coronary artery (RCA) was noted. Attempted cannulation of the RCA was difficult. Nonselective coronary angiography revealed aberrant dominant RCA arising from the left aortic sinus adjacent to the origin of the LCA (Figure 2). Selective coronary angiography of RCA showed anomalous origin from left aortic sinus; however, RCA had no significant stenotic lesions (Figure 3). The diagnosis of obstructive LAD lesion with anomalous origin of the RCA from the left aortic sinus was made. The LM artery was engaged with 6 French Judkins left 3.5 guiding catheter (Cordis). A 0.014 inch BMW (Abbott) guidewire was used to

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cross the lesion. An Integrity 3.5 x 18 mm bare metal stent (Medtronic) was deployed with final good result and Thrombolysis in Myocardial Infarction (TIMI) III flow (Figure 4). The patient's subsequent hospital stay was uneventful, and she was discharged home free of angina 3 days later. At 1 month follow-up, patient remained asymptomatic and a treadmill exercise test was negative for inducible myocardial ischemia.

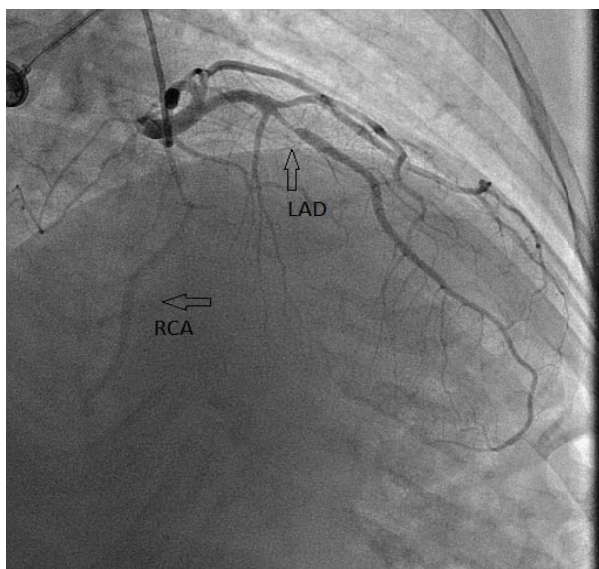


Figure 1. Selective coronary angiography of the left coronary artery (LCA) showed significant obstructive lesion in the mid part of the left anterior descending artery (LAD) just after the first diagonal branch, and also filling in the right coronary artery (RCA) was note

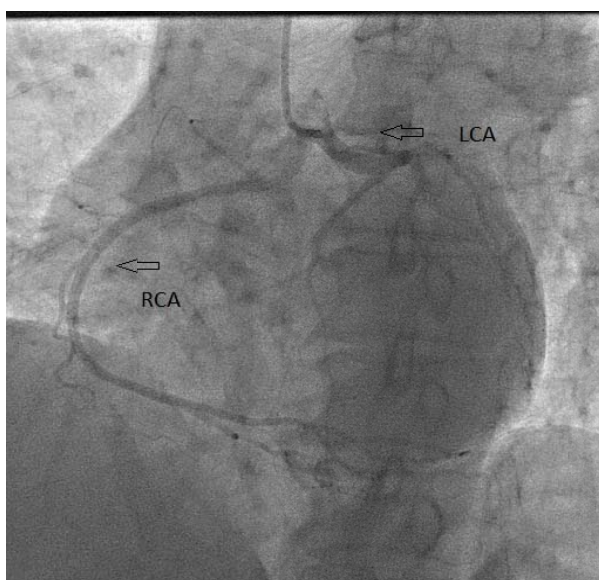


Figure 2. Nonselective coronary angiography revealed aberrant dominant right coronary artery (RCA) arising from the left aortic sinus adjacent to the origin of the left coronary artery (LCA)

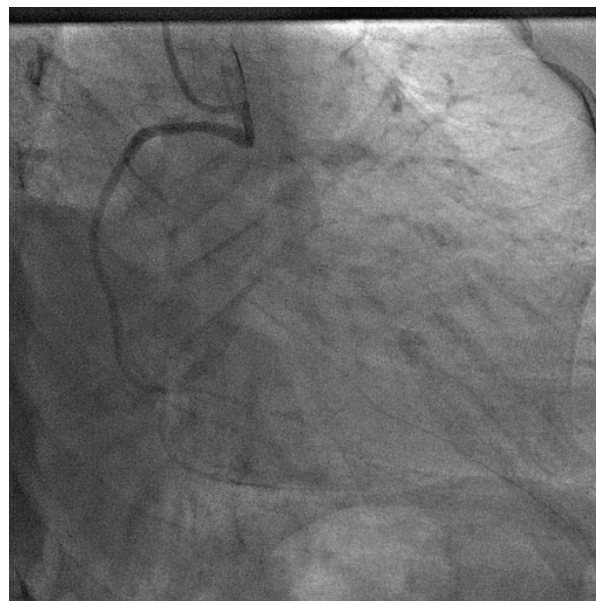


Figure 3. Selective coronary angiography of the right coronary artery from the left aortic sinus

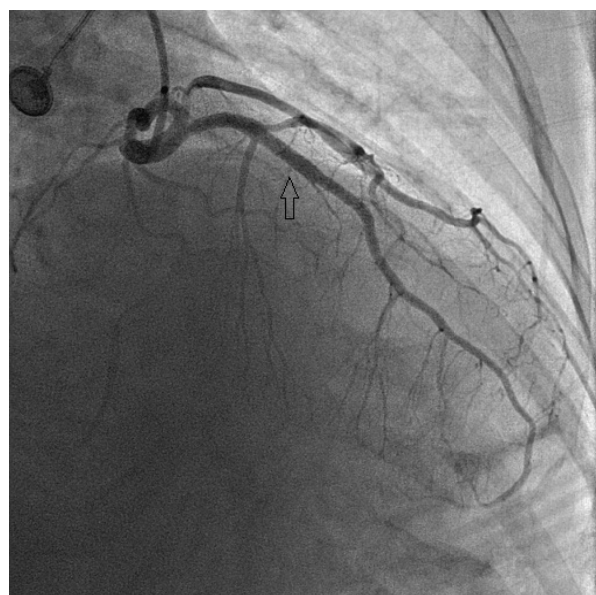


Figure 4. Final result after successful stent deployment in the left anterior descending artery (arrow)

Discussion

Anomalous origin of the right coronary artery (RCA) is a rare congenital anomaly that was first described in 1948 by White and Edwards.² Coronary artery anomalies are present in 1.3% of the population who undergo coronary angiography.¹ Of these, 90% are abnormalities of the origin of the coronary arteries, and the rest are coronary artery fistulas. Two-thirds of anomalous origins are the LCX arising from the right sinus and crossing behind the aorta, or the LAD and LCX arising separately from the left sinus. The other one-third

are aberrant origin of the RCA from the left sinus of Valsalva.

The incidence of anomalous RCA in congenital coronary anomalies is variable in different populations, with the highest incidence in Indian and the lowest incidence in German populations (0.46% and 0.04%, respectively).^{3,4} Angelini reported that the incidence of anomalous origination of the RCA from the left sinus is 0.92%.⁵ Kaku et al. examined 17,731 patients undergoing coronary angiography in Japanese centers between 1968 and 1994 and noted a prevalence of 0.25%.⁶

Most of the coronary anomalies remain asymptomatic and are incidental to investigations by coronary angiography. However, some have reported that an anomalous origin of the RCA can lead to angina pectoris, myocardial infarction, or sudden death even in the absence of atherosclerosis.⁶ The pathophysiologic basis for this association is unclear. Angina, infarction, or sudden death in these cases may be triggered by myocardial ischemia. The ischemia appears to be secondary to a combination of several factors that produce obstruction, such as mechanical compression of the RCA by the great vessels or the oblique angle at the juncture of the anomalous right coronary artery and a slit-like orifice in the aortic wall, which can collapse during exercise, produced by the left coronary sinus.⁶

Anomalous left main coronary artery as the cardiac anomaly has been shown to be associated with sudden cardiac death, but the choice of treatment in anomalous origin of RCA is controversial.⁷ Proposed options include translocation of the RCA to the aorta, ostioplasty, and bypass grafting of the RCA, with optional ligation of the native artery proximal to the graft anastomosis to prevent competitive flow.^{7,8} However, the long-term benefits of such therapies have not yet been demonstrated. Surgery in patients older than 35 years is not advised because sudden death mostly occurs before 35 years of age and the risk of sudden death decreases with age.^{8,9} In such cases the chief aim is good symptomatic relief. In a five year follow-up study in congenital coronary anomaly managed medically, no death was found to be directly related to the congenital anomaly.⁶

In conclusion, the congenital anomaly in this

case was an incidental finding, since the patient's initial clinical presentation was suggestive of significant atherosclerotic coronary heart disease. This case represents a rare case of anomalous origin of the RCA from the left sinus and successful PCI to severe stenosis at the mid LAD with good result.

Conflict of Interests

Authors have no conflict of interests.

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