Myocardial Perfusion Imaging in the Evaluation of Outcome of Coronary Intervention in Coronary Artery Disease Patients

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ABSTRACT

Objective: **Coronary artery disease (CAD) is an important medical and public health issue because it is one of the leading causes of death and disability throughout the world and is rapidly emerging as a major cause of mortality in developing countries including Bangladesh. SPECT-MPI is a cost- effective and non invasive means of identifying ischemic and viable myocardium along with its vascular distribution. This study is aimed to evaluate prospectively the ability of MPI to predict the outcome of Coronary Intervention in CAD patients of Bangladesh who are referred to National Institute of Nuclear Medicine & Allied Sciences (NINMAS) for performing MPI.**

Patients and Methods: **This prospective longitudinal and observational type of study was carried out in National Institute of Nuclear Medicine & Allied Sciences (NINMAS) located at Bangabandhu Sheikh Mujib Medical University (BSMMU) campus, from July 2017 to June 2018with 12 CAD patients who were referred here. Gated SPECT MPI was performed on the selected patients before any coronary intervention to predict myocardial viability & probable outcome of intervention. A follow up MPI of the same patients was performed after minimum 3 to 4 months of revascularization procedure to determine the outcome of intervention and to detect in stent restenosis or new onset ischemia if present which can be prevented by additional revascularization procedure. Finally pre and post intervention MPI results were analyzed by standard statistical analysis by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). P values <0.05 was considered as statistically significant.**

Results: **The sensitivity of MPI for the initial evaluation and risk stratification by diagnosing perfusion defect in the enrolled 12 CAD patients have been found to be 90%,77.8% and 81.8% in case of LAD, LCX and RCA territories respectively. Whereas, the specificity and positive predictive value have been found 100% for LAD and RCA territories. About 16.67% patients were found to have restenosis in this study diagnosed by early post-intervention MPI.**

It was observed that majority of the patients had perfusion defect in LAD territory. 3(25.0%) patients had fixed defect, 5(41.7%) patients had partial reversible defect and 4(33.3%) patients had complete reversible defect in pre intervention MPI. In post intervention MPI, 4(33.3%) patients had partially reversible perfusion defect, 2(16.7%) patients had fixed perfusion defect, 1(3.3%) patient was found with completely reversible perfusion defect and 5(41.7%) patients had normal MPI findings. The result was found statistically significant (P value <0.05) in case of partially reversible perfusion defect and normal MPI findings when before and after intervention MPI results were compared.

The difference of mean percentage of involved myocardium by fixed defect between pre and post intervention MPI was found statistically significant (P<0.05) in case of LAD territory and total LV myocardium involvement. 33.3% patients were in high risk before undergoing intervention, whereas it was found to be 25% after intervention which was calculated on the basis of their pre and post intervention Summed Stress Score (SSS) result.

Conclusion: **The results of this study have indicated that SPECT MPI provides significant independent information concerning the outcome of coronary intervention in CAD patients. Furthermore, early SPECT MPI after intervention successfully identified significant improvement of myocardial viability after revascularization in patients having complete or reversible perfusion defects found in pre intervention MPI along with identifying those having restenosis. It could also depict the reduction of percentage of myocardial fixed defects within 3-4 months after intervention which is also a positive outcome of coronary revascularization.**

Key words: **Myocardial Perfusion Imaging, Outcome of Coronary Intervention, Coronary Artery Disease patients.**

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INTRODUCTION

Coronary Artery Disease (CAD) is one of the major causes of death and disability in developed countries. Over past decade the mortality of CAD has declined however, it remains still high and responsible for about one third or more of all deaths in individuals over age 35 in United States.CAD is rapidly emerging as a serious health problem in developing countries including Bangladesh and evidence shows that it is becoming increasingly prevalent among younger people. Bangladesh is a small country with vast population (>160 million) with a limited health statistics. According to the latest WHO data published in May 2014 coronary heart disease deaths in Bangladesh reached 50,708 or 6.96% of total deaths. The age adjusted death rate is 53.53 per 100,000 of population ranks Bangladesh number 150th position in the world (World Health Rankings, May 2014).

The reduction in coronary artery flow in CAD may be symptomatic or asymptomatic. Myocardial ischemia or infarction may develop depending on severity and the rapidity of obstruction of coronary artery. Hence, early and accurate diagnosis is crucial and proper management is mandatory to increase the survival of the patient. Among the different investigation modalities available to assess the perfusion status of myocardium, SPECT-MPI is an effective and non invasive means of identifying ischemic and viable myocardium along with its vascular distribution. MPI plays a potential role in predicting the necessity of coronary intervention and also the probable outcome of intervention. The effectiveness of MPI in the follow-up of symptomatic and asymptomatic patients with PTCA has been defined by several studies. It is a cost saving procedure and has the ability to localize ischemia noninvasively and can detect stent restenosis.

SPECT Myocardial perfusion imaging is routinely performed at NINMAS, but no prospective data or study was conducted to assess the usefulness of SPECT MPI in patients with coronary artery disease before and after revascularization. This prospective study, before and after the coronary intervention, was aimed to provide the outcome of intervention and thereby to help in making rational management plan by the referring physicians.

PATIENTS AND METHODS

This prospective longitudinal and observational type of study was carried out in National Institute of Nuclear Medicine & Allied Sciences (NINMAS) located at Bangabandhu Sheikh Mujib Medical University (BSMMU) campus, from July 2017 to June 2018.Twelve CAD patients who were referred to NINMAS for gated SPECT MPI at various stages of clinical workup were selected for the study by purposive sampling technique. All patients underwent MPI performed with 99m Tc Sestamibi at first before undergoing coronary intervention. Single day stress - rest protocol was followed, according to the established practicing protocol of NINMAS. The patients were interviewed and complete clinical profile was recorded on the proposed questionnaire. All the patients were counseled briefly about the complete procedure and the possible side effects. Informed written consent was taken from the patients. All caffeine containing beverages were stopped for at least 24 hours and patients fasted for at least 4 hours before the stress study. Stress study was done by following one of the two following methods, 1) Exercise stress by treadmill following Modified Bruce protocol, 2) Pharmacological stress using Adenosine, Dobutamine or Dipyridamol. At stress the images were acquired on the dual headed SPECT gamma camera after 45 minutes of injection of 99m Tc Sestamibi (10-12 m Ci). Post stress acquisition with gating was done. Rest images were taken on the same day one hour after the injection of radiotracer at a higher dose (25-30mCi) of 99m Tc Sestamibi. Then the images were reconstructed and image analysis was done. Interpretation was done by two experienced nuclear medicine physicians and abnormalities were recorded, i.e: areas of perfusion defect, type of perfusion defect, SSS etc. Information also recorded from SPECT gating such as wall motion, LVEF, size of LV cavity, TID etc. The follow up MPI was performed at an interval of minimum 3-6 months after the coronary intervention procedure.

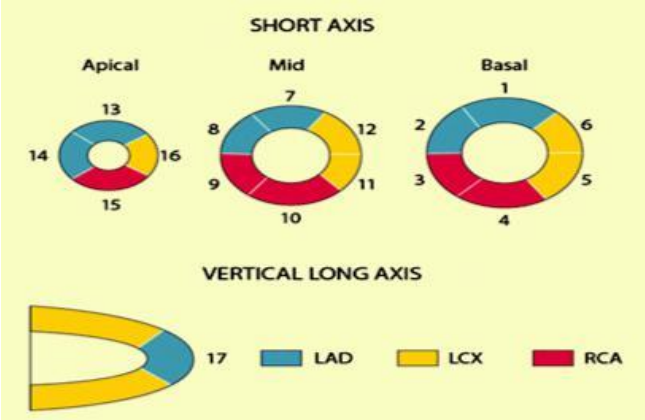

Figure 1: Standard model showing the 17 segments of the Coronary Arterial Territories corresponding to the Left Anterior Descending Artery (LAD), Right Coronary Artery (RCA) and Left Circumflex Artery (LCX). Adapted from the American Society of Nuclear Cardiology imaging guidelines for nuclear cardiology procedures: part 2,1999. Journal of Nuclear Cardiology, vol.6:, pp.G47-G48.

Finally pre and post intervention MPI results were analyzed by standard statistical analysis by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Paired t-test and Z-test were used for continuous variables. Chi-square test and Mc Nemer test were used to compare categorical data. P values <0.05 was considered as statistically significant.

RESULTS

The mean age of study patients was 55.58 ± 11.14 (mean ± SD) years. Among 12 participants 9 (75%) were male and 3 (25%) were female; data are shown in Table-1 and Table-2. Distribution of study patients by clinical complain is summarized in Table-3.

Table 1: Distribution of the study subjects by age (n=12)

Age (in years)	Number of patients	Percentage
40-50	4	33.3
51-60	4	33.3
>60	4	33.3
Mean±SD	55.58	±11.14
Range(min-max)	40	-79

Table 2: Distribution of the study subjects by sex (n=12)

Sex	Number	Percentage
Male	9	75.0
Female	3	25.0

Table 3: Distribution of the study subjects by clinical complain (n=12)

	Chest Discomfort		
	Present		Absent
	N	%	
With shortness of breath (SOB)	3	25.0	
Without SOB	7	58.3	
Total	10		2

A total of 10(83.3%) patients had perfusion defect in LAD territory, 8(66.7%) in LCX territory and 8(66.7%) in RCA territory. 3(25.0%) had fixed defect, 5(41.7%) patients had partial reversible defect and 4(33.3%) patients had complete reversible defect in pre intervention MPI (Table-4a and 4b). In pre-intervention MPI the sensitivity, specificity and positive predictive value of detecting perfusion defect in case of LAD territory are 90.0%, 100% and 100% respectively. In case of LCX territory they are 77.8%, 66.7% and 87.5% respectively. In case of RCA territory the sensitivity, specificity and positive predictive value are 81.8%, 100% and 100% respectively (Table-5).

Table 4 (a) : Distribution of the study subjects on the basis of involved coronary vascular territory in pre intervention MPI

Vascular Territory of Perfusion defect	Number	Percentage
LAD territory	10	83.3
LCX territory	8	66.7
RCA territory	8	66.7

Table 4 (b) : Distribution of the study subjects on the basis of type of perfusion defect in pre intervention MPI

Type of perfusion defect	Number	Percentage
Fixed defect	3	25
Partial reversible defect	5	41.7
Complete reversible defect	4	33.3

Table 5: Validity test of detecting perfusion defect in pre-intervention MPI compared to CAG.

Vascular territories having perfusion defect	Sensitivity (%)	Specificity (%)	Accuracy (%)	Positive predictive value (%)	Negative predictive value (%)
LAD in pre-intervention MPI	90.0	100.0	91.7	100.0	66.7
LCX in pre-intervention MPI	77.8	66.7	75.0	87.5	50.0
RCA in pre-intervention MPI	81.8	100.0	83.3	100.0	33.3

Table 6 summarizes the distribution of study patients by intervention. In post intervention MPI it was observed that 5(41.6%) patients had perfusion defect in LAD territory, 6(50%) in LCX territory and 5(41.6%) in RCA territory, 4(33.3%) patients had partially reversible perfusion defect, 2(16.7%) patients had fixed perfusion

defect, 1(3.3%) patient had completely reversible perfusion defect and 5(41.7) patients had normal MPI findings (Table-7). Table 8 shows the comparison between pre intervention and post intervention MPI findings of perfusion defects.

Table 6: Distribution of the study subjects by intervention (n=12)

Coronary vascular territory	Coronary intervention		
	PCI	CABG	PCI+CABG
LAD	3	1	1
LCX	5	1	0
RCA	3	0	0

Table 7: Distribution of the study subjects by involved vascular territory and type of perfusion defect in post intervention MPI study (n=12)

Vascular territory of Perfusion defect	Number	Percentage
LAD territory	5	41.6
LCX territory	6	50
RCA territory	5	41.6
Type of perfusion defect		
Fixed perfusion defect	2	16.7
Partial reversible perfusion defect	4	33.3
Complete reversible perfusion defect	1	8.3
Normal	5	41.7

Table 8: Comparisonbetween pre intervention and post intervention MPI findings of perfusion defects (n=12)

	Pre intervention MPI		Post intervention MPI				P value
			Perfusion defect present		Normal		
	N	%	N	%	N	%	
Fixed defect	3	25.0	2	16.7	1	20.0	>0.05
Partial reversibility	5	41.7	4	33.3	1	20.0	>0.05
Complete reversibility	4	33.3	1	8.3	3	60.0	>0.05

p value reached from Z-test

Table 9: Comparison between pre and post intervention MPI findings on the basis of involved coronary vascular territory (n=12)

Coronary vascular territory	Pre-intervention MPI					Post-intervention MPI					P-value
	No. of perfusion defect	Type of perfusion defect				No. of perfusion defect	Type of perfusion defect				
		Fixed	Complete reversible	Partial reversible	Mixed		Fixed	Complete reversible	Partial reversible	Mixed	
LAD	10 (27.7%)	3	3	3	1	5 (13.8%)	3	1	0	1	>0.05
LCX	8 (22.2%)	2	3	2	1	6 (16.6%)	3	1	0	2	
RCA	8 (22.2%)	1	5	1	1	5 (13.8%)	3	0	1	1	

Table 10: Comparison of percentage of involvement of myocardium by the fixed defects in preintervention MPI with post intervention MPI on the basis of involved vascular territory and total left ventricular myocardium (n=12)

	Percentage of Involvement of Myocardium				
	Pre Intervention		Post Intervention		P value
	Mean±SE	Range	Mean±SE	Range	
Fixed defect (LAD)	50.5±7.7	41-85	21.7±9.07	5-85	0.019^{S}
Fixed defect (LCX)	20.08±5.5	10-50	10.42±3.6	3-26	0.160^{ns}
Fixed defect (RCA)	31.75±10.8	5-95	9.0±4.1	8-45	0.104^{ns}
Fixed defect (total LV myocardium)	44.45±4.6	18-70	19.73±6.9	5-53	0.019^{S}

Table 11: Comparison of preintervention and post intervention MPI findings on the basis of Summed Stress Score (SSS) (n=12)

	Pre Intervention		Post Intervention		P value
	N	%	N	%	
Mild risk (<3 -8)	0	0.0	1	8.3	0.697^{ns}
Moderate risk (9 -13)	3	25.0	2	16.7	
High risk (>13)	4	33.3	3	25.0	

p value reached from Chi-square test

Table 12: Comparison of the study subjects by pre and post intervention MPI finding on the basis of LVEF (%) (n=12)

	Pre Intervention		Post Intervention		P value
	Mean	±SD	Mean	±SD	
MPI- LVEF stress	50.6	±13.2	57.1	±15.9	0.082^{ns}
Range (min-max)	26	,65	35	,72	
MPI- LVEF Rest	47.7	±11.2	55.0	±15.1	0.077^{ns}
Range (min-max)	29	,65	33	,72	

p value reached from paired t-test

Table 13: Comparison between pre and post intervention MPI SPECT gating findings(n=12)

	Pre Intervention		Post Intervention		P value
	N	%	n	%	
MPI- Wall motion					
Normal	6	50.0	7	58.3	
Abnormal	6	50.0	5	41.7	1.000^{ns}
MPI- Wall Thickening					
Normal	8	66.7	8	66.7	1.000^{ns}
Wall thinning	4	33.3	4	33.3	1.000^{ns}
MPI- LV cavity					
Normal	8	66.7	8	66.7	
Borderline Dilated	2	16.7	3	25.0	1.000^{ns}
Dilated	2	16.7	1	8.3	
MPI- TID					
Normal	9	75.0	8	66.7	
Higher	3	25.0	4	33.3	0.653^{ns}
MPI-Cardiomyopathy					
Absent	8	66.7	8	66.7	
Present	4	33.3	4	33.3	1.000^{ns}

p value reached from McNemar test

Table- 14: Distribution of the study subjects by history of restenosis in CAG and Post-intervention MPI (n=12)

History of restenosis in CAG	Number of patients	Percentage	History of restenosis in MPI	Number of patients	Percentage
Present	**4**	**33.33**	**Present**	**2**	**16.67**
Absent	**8**	**66.67**	**Absent**	**10**	**83.33**

DISCUSSION

At the beginning 22 patients were enrolled according to selection criteria. 2 patients died during the study period before undergoing post-intervention MPI, 4 patients did not undergo coronary intervention even after being advised by their respective physicians and 4 patients did not come for follow up MPI after intervention within the study period. After excluding these 10 patients we completed the study with 12 CAD patients. The mean age of study patients was 55.58 ± 11.14 (mean ± SD) years of whom 9 (75%) were male.

The result of pre-intervention MPI revealed the perfusion defect was mostly found in LAD territory which was about 83.3%. It was also observed in the study of LeBlanc et al. 2016, where LAD territory was involved in 60% of STEMI patients and 96% of chronic stable angina patients (1).The sensitivity of pre intervention MPI for the initial evaluation and risk stratification by diagnosing perfusion defect in these patients have been found to be 90%, 77.8% and 81.8% in case of LAD, LCX and RCA territories respectively. Whereas the specificity and positive predictive value have been found 100% for LAD and RCA territories compared to Coronary Angiography being the gold standard (Table-5). The overall performance of SPECT-MPI for the detection of myocardial ischemia was 79% for both sensitivity and specificity in a study done by Galassi et al. 2011 (2). The meta-analysis of Takx et al. shows that sensitivity and specificity of SPECT MPI is 74% and 79% respectively (3). In the present study, the sensitivity, specificity and positive predictive value were found higher as the pre intervention MPI was performed within 3-4 months after coronary angiography in most of the patients. The use of stress nuclear imaging increases significantly the sensitivity of detecting perfusion defect to 87% and the specificity to 78% (4). So, it is more favorable to take the coronary intervention decisions considering the MPI results as it can predict the perfusion defects more specifically. Present study shows similar results establishing SPECT MPI as the most reliable non invasive method in diagnosing significant perfusion defect in known or suspected CAD patients and whether they can be improved by revascularization or not.

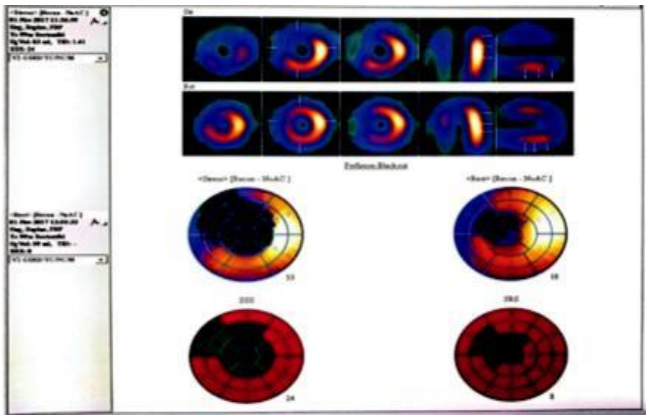

Figure 2: The photograph of pre intervention MPI of a 46 years old male CAD patient showing large fixed perfusion defect with large area of peri-infarct ischemia involving LAD territory and reversible perfusion defect in LCX and RCA territories representing ischemia

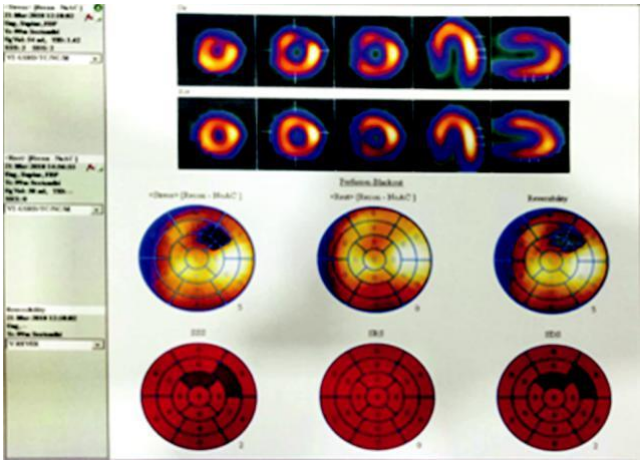

Figure 3: The photograph of post-intervention MPI of the same patient after 3 months of undergoing PTCA with stenting to LAD showing very small reversible perfusion defect in LAD & LCX territories represent ischemia.

Approximately 60% of patients with completely reversible perfusion defect in pre-intervention MPI had normal findings in follow up MPI done after intervention and 20% patients having partially reversible perfusion defects in pre-intervention MPI had normal finding in follow up MPI (Table-8). SPECT myocardial perfusion imaging provided significant prognostic information for the prediction of outcome in these patients. In a previous study done on known or suspected CAD patients undergoing MPI in 2012 about 08% patients had completely reversible perfusion defects, 12% had partially reversible perfusion defects and 30% had fixed perfusion defects before undergoing intervention. During a follow up of 9.2 ± 2 years it was observed that patients with an abnormal SPECT study had a significantly increased MACE (Major Advance Cardiac Events) rate as compared with patients who had normal MPI results previously (5). Before intervention the mean percentage of involved myocardium by fixed defect in LAD territory was 50.5 ± 7.7 with ranged from 41% to 85% and after intervention the mean percentage was 21.7

± 9.07 with ranged from 05% to 85% (Table-10). In case of total LV myocardial involvement the mean percentage of fixed defect also significantly reduced in post intervention MPI than the pre intervention MPI. These two results are statistically significant which depicts the positive outcome of coronary intervention on fixed defect.

Risk stratification using myocardial perfusion SPECT Summed Stress Score (SSS) has been proved to be crucial by providing incremental information over clinical data for prediction of outcome. SSS is considered to be an independent predictor of MACE (Major Adverse Cardiac Events) (6). It is obtained by adding the scores of the 20 segments of the stress Tc99m Sestamibi SPECT images. A summed stress score of <4 is considered normal, 4-8 is mildly abnormal and >8, severely abnormal.6 In this study it was observed that 33.3% patients were in high risk before undergoing intervention, whereas it was found to be 25% after intervention in these patients (Table-11).

Among total 12 patients, 04 patients had undergone CAG after intervention and found to have developed restenosis. 02(16.67%) patients had perfusion defect in the stented vascular territory in post intervention MPI which can be regarded as restenosis (Table-14). That helped the physicians in making further management plan in these patients i.e whether to go for coronary intervention again or not. The incidence of development of restenosis was found to be 31% in a study by Galassi et al. 2000 where SPECT MPI was performed after 5-6 months of coronary intervention (7). Post intervention MPI has been performed mostly after 3-4 months in current study which may have influenced the lower percentage of re-stenosis compared to the previous study. Also, if we could include the post intervention CAG result in all the study subjects then we could have better scenario of sensitivity of detecting restenosis in post intervention MPI in present study.

SPECT MPI has disadvantages as radiation exposure to the patient and higher costs. Radiation exposure is an increasingly relevant topic as myocardial perfusion SPECT studies are an important source of medical radiation exposure and because patients frequently have multiple procedures performed over time. It is said that new cadmium zinc telluride SPECT camera technology may substantially reduce radiation exposure while

maintaining image quality (8). Moreover, an individualized imaging protocol may further reduce both study time and radiation exposure. If the patients have normal stress myocardial perfusion images, then in these patients resting images are not necessary and a further reduction in the radiation dose can be achieved by using a stress-only imaging protocol (9).Cost is another factor limiting routine risk stratification using myocardial perfusion SPECT when compared with other non-invasive methods i.e exercise electrocardiographic testing. But suboptimal accuracy of exercise electrocardiographic testing may result in potential misdiagnosis of obstructive coronary artery disease, which may hinder appropriate patient care. Additionally, myocardial perfusion SPECT has a high negative predicting value, which may avoid the use of unnecessary (invasive) diagnostic procedures (9). In previous studies it has been found that the costs were significantly lower after using SPECT MPI rather than CTA or PET in the evaluation of suspected coronary disease. SPECT has been found to be economically attractive compared with PET, whereas CTA was associated with higher costs and also there was no significant difference in mortality compared with SPECT (10).

CONCLUSION

The results of this study have indicated that SPECT MPI provides significant independent information concerning the outcome of coronary intervention in CAD patients. The sensitivity of predicting the outcome of post coronary intervention is >75% in all 3 major coronary vascular territories, whereas the specificity and PPV both are 100% in 2 out of 3 major vascular territories. Furthermore, early SPECT MPI after intervention successfully identified significant improvement of myocardial viability after revascularization in patients having complete or reversible perfusion defects found in pre intervention MPI along with identifying those having restenosis. It could also depict the reduction of percentage of myocardial fixed defects within 3-4 months after intervention which is also a positive outcome of coronary revascularization.

RECOMMENDATION

Future studies with large number of study subjects should be performed for better specification of this result.

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