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Temporal trends in results of 9170 myocardial perfusion imaging studies (2004 to 2013)

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Abstract

BACKGROUND: To assess the frequency of normal and abnormal myocardial perfusion imaging (MPI) in a consecutive cohort of patients from Pakistan over a period of 8.5 years.

MATERIAL AND METHODS: We assessed 9170 patients who had undergone stress-rest MPI between January 2004 and June 2013. Patients were assessed for change in demographics, risk factors, and frequency of abnormal and normal MPI.

RESULTS: Overall mean age and male predominance of studied cohort was ≈ 55 years and $\approx 55:45$ (M:F), respectively, with no appreciable decline or rise. Marked decline in exercise as mode of stress (from 71% to 35%, p value significant) was noted during the study period. Regarding the risk factors for CAD, only hypertension was noted to have a significant rising trend during the study period. Trend of MPI results over study period was found non-significant from 2004 till 2006 but from 2007 onward (except 2008), a marginal but significant decline in abnormal MPIs (from 45% to 42%; significant p value) and rise in normal MPI (from 55% to 58%; significant p value) was noted.

CONCLUSIONS: We conclude that over the past 8.5 years, a marginal but significant decline in abnormal and a rise in normal MPIs trend have been observed. An exorbitant rise in use of vasodilator as a method of stress was also observed. We envisaged a follow-up study to ascertain lower negative predictive value of vasodilator as a possible reason and till then results of this and other such studies must be read cautiously.

KEY words: myocardial perfusion imaging, temporal trends, negative predictive value, normal MPI, abnormal MPI

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Background

Myocardial perfusion imaging (MPI) using ECG-gated single photon emission computerized tomography (GSPECT) since its introduction in late 1980s has become the most commonly performed non-invasive functional cardiac imaging modality. This is attributed as it provides enormous information for risk assessment of patients with known or suspected coronary artery disease and aids in the assessment of myocardial viability [1]. According to 2010 statistic published by American Heart Association (AHA), there has been a progressive decline in cardiac deaths and myocardial infarction,

yet the burden of disease remain high [2]. A recently published single center study from USA has documented a declining trend of abnormal GSPECT over a period of two decades [3]. However, despite the high death rates due to non-communicable diseases, by 2010 the leading cause of death in the developing countries including Pakistan would be cardiac deaths [4]. With this diversified pattern of cardiac mortalities, the purpose of this study was to assess the frequency of normal and abnormal MPIs in a consecutive cohort of patients from Pakistan over a period of 8.5 years.

Material and methods

This study included 10 563 consecutive patients who had GSPECT studies at Karachi Institute of Radiotherapy and Nuclear Medicine [KIRAN] (3905 patients from January 2004 till November 2009) and Karachi Institute of Heart Diseases [KIHD] (6658 patients from December 2009 till June 2013). We excluded 1393

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patients with history of valvular disease and cardiomyopathies, while remaining 9170 patients constituted the studied cohort. The study was duly approved by ethical review committee of Institutes. As per departmental practice, pertinent information regarding demographics, presenting complaints, risk factors, and history of intervention were recorded. Dynamic exercise (Bruce or Modified Bruce Protocol) was used in 4469 patients (48.74%) and remaining 4701 (51.26%) patients had pharmacological stress using dipyridamole (with or without low level exercise). SPECT MPI was acquired using one day stress and rest or stress only without gating (3905 patients from January 2004 till November 2009) and with gating (6658 patients from December 2009 till June 2013) using 16 frames for post-stress studies under dual head gamma cameras (CardioMD, Philips, Netherland and Mediso, Hungry till November 2009 and only CardioMD, Philips, Netherland from December 2009 onward). Technetium-99m labelled Methoxy IsoButyl Isonitrile (Tc-99m MIBI) in dose of 10–15 mCi (370–555 MBq) for stress and 20–30 mCi (740–1110 MBq) for resting studies. Radiotracer was injected at least 1 minute before terminating the treadmill stress test and 3 minutes after dipyridamole infusion (0.142 mg/kg/min for 4 minute). We did not use attenuation correction in either study. Left ventricular function parameters like ejection fraction (LVEF in %), end-diastolic volume (EDV in ml) and end-systolic volume (ESV in ml) were measured using commercially available software (Autoquan®). All patients were asked to come with 3–4 hour fasting, stop beta and calcium blocker 24 hours prior, long acting nitrate and tea/coffee at least 12 hour prior the test. All scans were reported by two board certified nuclear cardiologists with > 05 years' experience.

Statistical analysis

Data was analyzed by using the MedCalc statistical software version 11.3.10 and SPSS software version 10. Comparisons between patient groups were performed using Student's t test for continuous variables and the χ^2 test for categorical variables. Continuous variables were described by mean \pm standard deviation (SD). Odd ratios with 95% confidence intervals (CIs) were calculated. Statistical significance was defined as $p < 0.05$.

Results

The overall mean age and male predominance of studied cohort over the last 8.5 years was \approx 55 year and \approx 55:45 (M: F) respectively with no appreciable decline or rise. Obesity (BMI > 27) was found in 1957 (21.03%) of studied cohort with a significant rise during the study period. A significant decline in exercise as mode of stress was noted during the study period. Regarding the risk factors for CAD, only hypertension was noted to have a significant rising trend during the study period, while rest of risk factors did not show any significant shift. Incidence of CAD did also show a significant declining trend during the study period (Table 1, Figure 1). Regarding the trends of MPI results over study period, it was found non-significant from 2004 till 2006 but from 2007 onward (except 2008), a marginal but significant decline in abnormal MPIs was noted (Table 1 and Figure 2).

Comparing the patients' cohort with normal and abnormal MPI each study year, patients with abnormal MPIs were found to be significantly older with male predominance and lower BMI

Table 1. Patients' characteristics

Variables	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Total	685	637	690	791	1279	1049	1159	909	1333	638
Age \pm SD	55 \pm 11	54 \pm 10	54 \pm 10	53 \pm 10	55 \pm 11	55 \pm 11	55 \pm 11	55 \pm 10	56 \pm 10	56 \pm 11
Male	394	358	362	447	753	571	632	505	738	350
Female	291	279	328	344	526	478	527	404	595	288
M:F	58:42	56:44	52:48	57:43	59:41	54:46	55:45	56:44	55:45	55:45
BMI	24.87 \pm 5.25	26.32 \pm 5.99	26.38 \pm 8.53	26.58 \pm 7.42	25.75 \pm 4.64	26.53 \pm 4.97	27.73 \pm 9.62	27.98 \pm 9.84	27.27 \pm 4.93	27.20 \pm 4.48
Obese	109	133	135	120	187	195	313	243	365	157
HTN	437	374	419	517	889	718	789	630	972	467
DM	252	207	252	277	500	390	454	357	518	265
Dyslip	207	158	201	252	423	328	401	306	450	231
FH of CAD	224	235	245	280	445	292	371	325	499	221
Smoking	132	118	101	142	200	169	160	145	246	110
CAD	252	177	144	155	288	249	232	201	262	149
Exercise	484	472	448	498	734	553	482	245	332	221
Dipyridamole	201	165	242	293	545	496	677	664	1001	417
METS	7.43 \pm 2.39	7.84 \pm 4.60	8.01 \pm 2.39	8.36 \pm 3.87	8.38 \pm 5.31	8.45 \pm 6.62	8.09 \pm 1.98	8.21 \pm 5.23	8.88 \pm 2.27	7.55 \pm 2.19
%THR	84 \pm 10	84 \pm 11	86 \pm 10	86 \pm 12	87 \pm 10	86 \pm 10	86 \pm 10	86 \pm 10	88 \pm 10	87 \pm 12
Normal MPI	358	344	365	448	670	581	694	555	776	369
Abnormal MPI	327	293	325	343	609	468	465	354	557	269
%LVEF	58 \pm 16	58 \pm 18	60 \pm 18	59 \pm 15	58 \pm 16	59 \pm 16	59 \pm 15	58 \pm 15	59 \pm 23	58 \pm 17
EDV	99 \pm 50	101 \pm 52	96 \pm 49	101 \pm 79	101 \pm 50	99 \pm 51	99 \pm 49	98 \pm 69	99 \pm 52	93 \pm 47
ESV	47 \pm 44	48 \pm 45	45 \pm 44	47 \pm 44	48 \pm 46	45 \pm 43	46 \pm 44	43 \pm 41	45 \pm 44	45 \pm 40

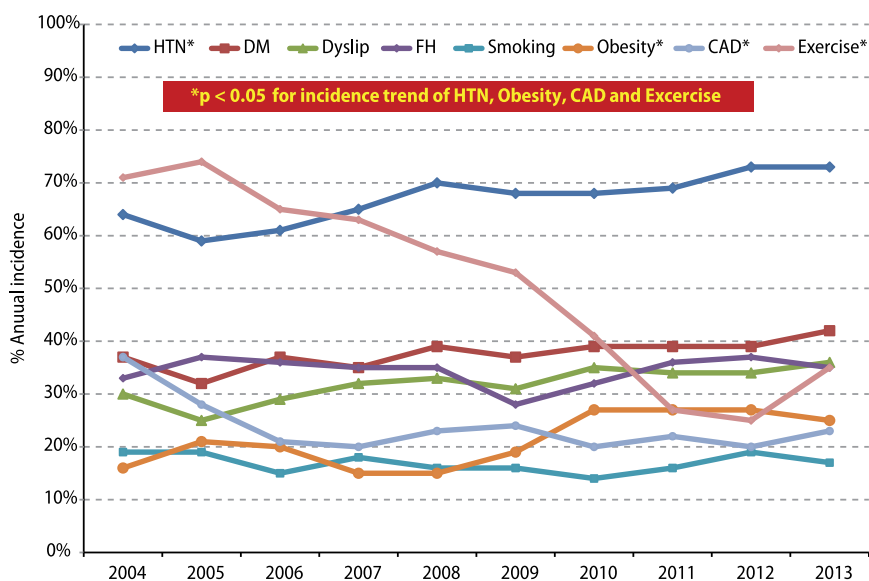


Figure 1. Demographical overall annual incidence trend (%) from 2004 to 2013

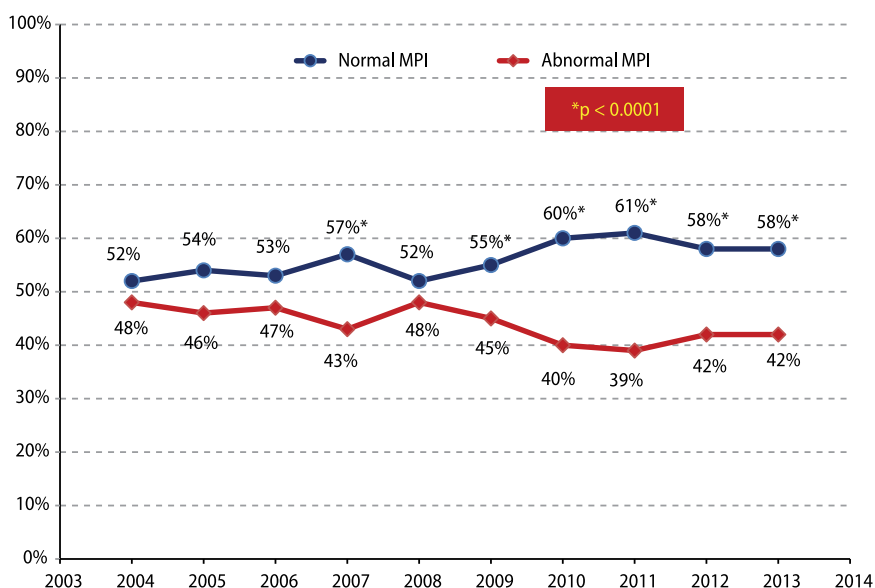


Figure 2. Annual incidence trend (%) for normal and abnormal myocardial perfusion imaging (2004 to 2013)

(except in 2004 and 2007). Regarding the risk factors, patients with abnormal MPIs were found to have significantly higher prevalence of diabetes and smoking but significant lower prevalence of hypertension (except in 2006). A non-significant prevalence was found for dyslipidemia (except 2005) and family history (except 2004 and 2010) between patients with normal and abnormal MPIs in each study year (Table 2). In patients with normal MPIs, exercise as mode of stress shows a significant declining trend, while hypertension, diabetes, dyslipidemia, family history, smoking, obesity and CAD did not show any significant change in trend over the study period (Table 2 and Figure 3). In patients with abnormal MPIs, a significant declining trend was noted for exercise as mode of stress and presence of CAD, significantly rising trend was observed for diabetes and hypertension, while no significant change in trend was noted for rest of attributes (Table 2 and Figure 4). We have also estimated

odds ratio for predicting an abnormal MPI in studied period, and significant odd ratios were estimated for male gender, smoking and CAD for abnormal and normal MPI (Table 3).

Discussion

In this study we have observed a mild but significant declining trend of abnormal MPIs in the second half of study period. There was a concomitant significant increase in mean BMI of all participants, which is considered to have a positive correlation with CAD and associated mortality [5]. However, there are published studies revealing low incidence of abnormal MPIs in obese patients [6] and plausible explanation for this protective role of higher BMI is reverse epidemiology and obesity paradox [7]. We have also observed an overall significant declining trend of exercise as a mode

Table 2. Yearly comparative analysis between normal and abnormal myocardial perfusion imaging

Variables	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Total	685	637	690	791	1279	1049	1159	909	1333	638
Normal:	358:	344:	365:	448:	670:	581:	694:	555:	776:	369:
Abnormal	327	293	325	343	609	463	465	354	557	269
Age	Normal 52 ± 10	Normal 52 ± 11	52 ± 10	52 ± 11	53 ± 11	54 ± 11	55 ± 10	54 ± 11	55 ± 10	55 ± 11
	Abnormal *57 ± 10	Abnormal *56 ± 10	*56 ± 10	*56 ± 10	*57 ± 10	*57 ± 10	56 ± 11	*58 ± 11	*58 ± 10	*57 ± 10
M:F%	Normal 40:60	42:58	37:63	40:60	46:54	40:60	40:60	44:56	43:57	46:54
	Abnormal *76:24	*73:27	*70:30	*78:22	*73:27	*72:28	*77:23	*76:24	*72:28	*68:32
BMI	Normal 25.23 ± 6.26	27.09 ± 5.89	26.93 ± 5.07	26.68 ± 5.48	26.43 ± 4.73	27.17 ± 5.25	27.98 ± 5.17	28.81 ± 5.81	27.84 ± 5.13	27.59 ± 4.68
	Abnormal 24.48 ± 5.15	*25.38 ± 5.77	*25.77 ± 7.59	26.44 ± 4.98	*24.99 ± 4.41	*25.69 ± 4.41	27.38 ± 4.81	*26.69 ± 4.45	*26.47 ± 4.52	*26.67 ± 4.14
Obese	Normal 65 (18%)	*92 (27%)	*95 (26%)	*86 (19%)	*125 (19%)	*147 (25%)	*221 (32%)	*172 (31%)	*252 (32%)	*103 (28%)
	Abnormal 44 (13%)	41 (14%)	40 (12%)	34 (10%)	62 (10%)	48 (10%)	92 (20%)	71 (20%)	113 (20%)	54 (20%)
HTN	Normal *252 (70%)	*226 (66%)	231 (63%)	*308 (69%)	*490 (73%)	*425 (73%)	*497 (72%)	*405 (73%)	*593 (76%)	*287 (78%)
	Abnormal 185 (57%)	148 (51%)	188 (58%)	209 (61%)	399 (66%)	293 (63%)	292 (63%)	225 (64%)	379 (68%)	180 (67%)
DM	Normal 115 (32%)	98 (28%)	116 (32%)	141 (31%)	243 (36%)	195 (34%)	256 (37%)	186 (34%)	283 (36%)	130 (35%)
	Abnormal *137 (42%)	*109 (37%)	*136 (42%)	*136 (40%)	*257 (42%)	*195 (42%)	*198 (43%)	132 (37%)	*235 (42%)	*135 (50%)
Dyslip	Normal 116 (32%)	*98 (28%)	111 (30%)	147 (33%)	215 (32%)	189 (33%)	254 (37%)	195 (35%)	272 (35%)	131 (36%)
	Abnormal 91 (28%)	60 (20%)	90 (28%)	105 (31%)	208 (34%)	139 (30%)	147 (32%)	111 (31%)	178 (32%)	100 (37%)
F/H	Normal 138 (39%)	136 (40%)	136 (37%)	170 (38%)	242 (36%)	163 (28%)	227 (33%)	202 (36%)	288 (37%)	134 (36%)
	Abnormal *86 (26%)	99 (34%)	109 (34%)	110 (32%)	203 (33%)	129 (28%)	*224 (48%)	123 (35%)	211 (38%)	87 (32%)
Smoking	Normal 45 (13%)	40 (11%)	30 (08%)	46 (10%)	69 (10%)	58 (10%)	68 (10%)	72 (13%)	117 (15%)	51 (14%)
	Abnormal *87 (27%)	*78 (27%)	*71 (22%)	*96 (28%)	*131 (22%)	*111 (24%)	*92 (20%)	*73 (21%)	*129 (23%)	*59 (22%)
CAD	Normal 60 (17%)	54 (16%)	33 (9%)	35 (8%)	81 (12%)	68 (12%)	75 (11%)	77 (14%)	88 (11%)	45 (12%)
	Abnormal *192 (59%)	*123 (42%)	*111 (34%)	*120 (35%)	*207 (34%)	*181 (39%)	*157 (34%)	*124 (35%)	*174 (31%)	*104 (39%)
Exercise	Normal 260 (73%)	256 (74%)	244 (67%)	289 (65%)	378 (56%)	280 (48%)	250 (36%)	145 (26%)	203 (26%)	*146 (40%)
	Abnormal 224 (69%)	216 (74%)	204 (63%)	209 (61%)	356 (58%)	*273 (58%)	*232 (50%)	100 (28%)	129 (23%)	75 (28%)
Dipyridamole	Normal 98 (27%)	88 (26%)	121 (33%)	159 (35%)	292 (44%)	301 (52%)	444 (64%)	410 (74%)	574 (74%)	223 (60%)
	Abnormal 103 (31%)	77 (27%)	121 (37%)	134 (39%)	253 (42%)	195 (42%)	233 (50%)	254 (72%)	427 (77%)	194 (72%)
METS	Normal 7.71 ± 2.37	8.08 ± 2.19	8.63 ± 2.25	8.59 ± 2.97	9.12 ± 4.25	9.07 ± 7.43	8.53 ± 1.99	8.89 ± 6.66	8.74 ± 2.10	8.01 ± 2.03
	Abnormal 7.11 ± 2.37	7.55 ± 5.39	*7.27 ± 2.21	8.05 ± 5.22	*7.59 ± 2.23	*7.82 ± 5.59	*7.62 ± 1.85	*7.22 ± 1.87	*7.96 ± 2.05	*6.67 ± 2.23
%THR	Normal 86 ± 09	86 ± 09	88 ± 10	87 ± 10	89 ± 10	89 ± 08	88 ± 09	88 ± 10	87 ± 12	88 ± 11
	Abnormal *82 ± 10	*82 ± 12	*84 ± 9	*83 ± 16	*84 ± 11	*83 ± 10	*84 ± 10	*84 ± 10	*84 ± 12	*84 ± 12
%LVEF	Normal 67 ± 10	67 ± 14	69 ± 09	67 ± 09	67 ± 09	69 ± 09	67 ± 10	65 ± 11	66 ± 11	65 ± 14
	Abnormal *48 ± 15	*47 ± 16	*49 ± 20	*47 ± 15	*48 ± 15	*48 ± 15	*47 ± 13	*46 ± 14	*48 ± 32	*45 ± 15
EDV	Normal 77 ± 29	76 ± 30	73 ± 24	77 ± 30	79 ± 25	76 ± 27	78 ± 26	79 ± 32	80 ± 27	76 ± 26
	Abnormal *125 ± 56	*130 ± 58	*124 ± 57	*133 ± 108	*127 ± 59	*127 ± 60	*130 ± 58	*130 ± 99	*130 ± 66	*127 ± 59
ESV	Normal 27 ± 21	26 ± 24	24 ± 18	27 ± 23	26 ± 18	25 ± 19	26 ± 18	28 ± 24	28 ± 22	27 ± 21
	Abnormal *70 ± 51	*75 ± 53	*72 ± 58	*74 ± 54	*73 ± 54	*71 ± 50	*75 ± 54	*70 ± 50	*75 ± 54	*73 ± 47

*p < 0.05; M = male, BMI = body mass index, F = female, METs = metabolic equivalent tasks, HTN = hypertension, THR = target heart rate, DM = diabetes mellitus, LVEF = left ventricular ejection fraction, Dyslip = dyslipidemia, EDV = end diastolic volume, FH = family history, ESV = end systolic volume, SMK = smoking, CAD = coronary artery disease

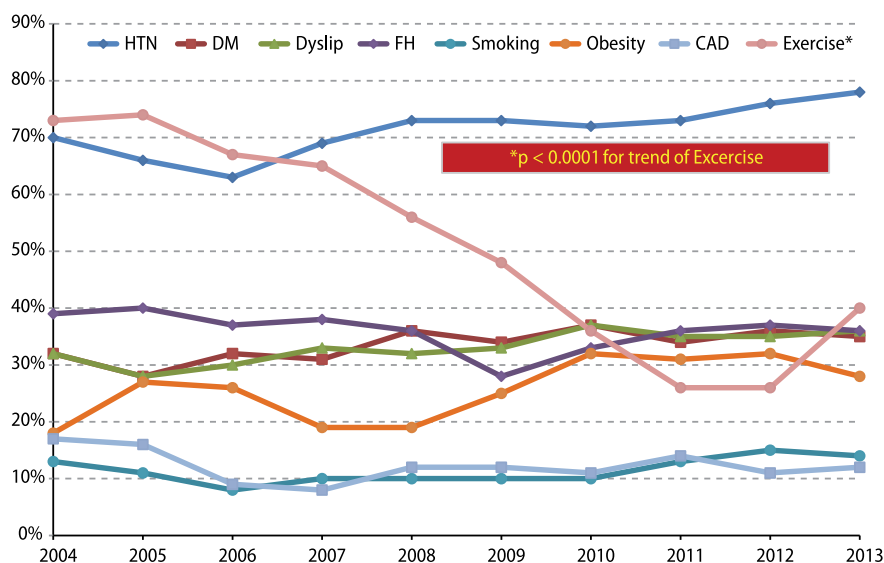


Figure 3. Demographical annual %incidence trend from 2004 to 2013 for normal MPI

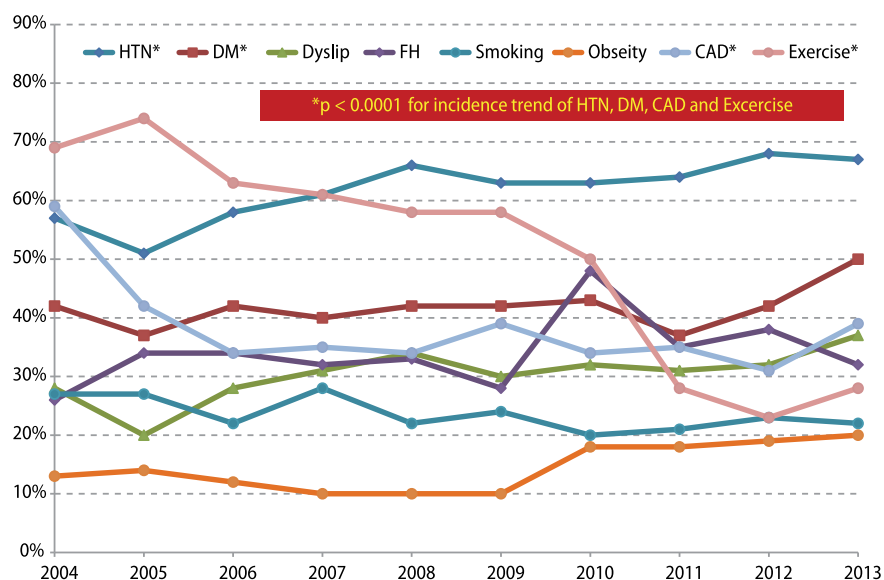


Figure 4. Demographical annual %incidence trend from 2004 to 2013 for abnormal MPI

of stress, and a sedentary life style in studied population could be the prime reason for preference towards pharmacological (vasodilator) intervention over exercise as stress method. It is generally considered that MPI results obtained with vasodilators stress have shown good concordance with exercise stress [8, 9]. However, recent studies have shown lower negative predictive value (NPV) of a normal MPI done with vasodilator than with dynamic exercise [10, 11]. We cannot exclude possible contribution of higher false negative results to the rising trend of normal MPIs in our cohort, as coronary angiography was not justified in these cases. Our results are in concordance with a study published by Rozanski et al. [3], although their study exhibited a very steep declining trend of abnormal MPIs from 40.9% to 8.7% in 20 years. The primary reason could be the larger sample size and longer study duration in their study.

Comparing patients with normal and abnormal MPIs on yearly basis, older age, male gender predominance, lower BMI,

diabetes and smoking were found to have significant correlation with abnormal than normal MPIs. Except lower BMI, the remaining are well established risk factors for CAD and favor contribution towards an abnormal MPI. Reverse epidemiology and obesity paradox as discussed above may be the possible reasons for an unusual association between lower BMI and abnormal MPIs, which needs to be explored appropriately.

Interestingly in patients' cohort with a marginal rising trend of normal MPIs, only dynamic exercise did show an exaggerated declining trend while rest of known risk factors did not do exhibit any significant change in trend. The possible explanation could be the referral bias or possible higher false negative rate (lower NPV) of vasodilator stress MPI [12]. While marginal but significant declining trend of abnormal MPIs was found to be associated with significant rising trend of DM and HTN. This finding is in contradiction to previous studies where significant decline in abnormal MPIs was associated with reduction in risk factors [3]. One plausible

Table 3. Odd ratios as predictor for abnormal MPIs

Between abnormal and normal MPI	Odd Ratios (OR) (95% Confidence interval; lower-upper limits)										
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	
M:F	4.856* (3.488-6.761)	3.762* (2.960-5.261)	4.005* (2.912-5.508)	5.370* (3.906-7.382)	3.189* (2.522-4.033)	3.869* (2.979-5.026)	5.006* (3.845-6.519)	4.034* (3.000-5.423)	3.402* (2.694-4.295)	2.491* (1.794-3.457)	
Non-obese:	1.423 (0.941-2.163)	2.243* (1.493-3.372)	2.506* (1.672-3.759)	2.159* (1.141-3.303)	2.026* (1.456-2.806)	2.694* (2.084-4.216)	1.894* (1.434-2.503)	1.790 (1.305-2.456)	5.818* (4.603-7.358)	1.542 (1.059-2.244)	
HTN	0.548 (0.399-0.751)	0.533 (0.387-0.734)	0.796 (0.586-1.081)	0.709 (0.528-0.952)	0.698 (0.549-0.886)	0.615 (0.472-0.799)	0.669 (0.521-0.859)	0.646 (0.485-0.860)	0.657 (0.515-0.838)	0.578 (0.406-0.823)	
DM	1.524 (1.115-2.081)	1.487 (1.066-2.047)	1.545 (1.131-2.109)	1.431 (1.066-1.919)	1.283 (1.024-1.607)	1.414 (1.099-1.819)	1.269 (0.998-1.612)	1.179 (0.893-1.558)	1.271 (1.017-1.589)	1.852 (1.344-2.552)	
Dyslip	0.804 (0.579-1.117)	0.646 (0.447-0.934)	0.876 (0.630-1.219)	0.903 (0.667-1.223)	1.097 (0.869-1.386)	0.876 (0.673-1.141)	0.801 (0.642-1.027)	0.843 (0.634-1.121)	0.870 (0.691-1.097)	1.075 (0.775-1.490)	
FH	0.569 (0.411-0.788)	1.081 (0.773-1.514)	0.849 (0.621-1.162)	0.772 (0.574-1.083)	0.884 (0.702-1.134)	0.976 (0.744-1.281)	1.912* (1.502-2.434)	0.931 (0.704-1.229)	1.033 (0.825-1.294)	0.838 (0.601-1.169)	
SMK	2.521* (1.695-3.751)	2.752* (1.819-4.193)	3.121* (1.967-4.929)	3.397* (2.310-4.994)	2.387* (1.712-3.272)	2.807* (1.986-3.959)	2.271* (1.618-3.189)	1.742* (1.219-2.491)	1.698* (1.585-2.242)	1.752* (1.589-2.648)	
CAD	7.064* (4.957-10.065)	3.886* (2.697-5.635)	5.218* (3.412-7.981)	6.349* (4.213-9.570)	3.251* (2.446-4.319)	4.756* (3.475-6.513)	4.207* (3.094-5.719)	3.347* (2.418-4.632)	3.552* (2.671-4.724)	4.538* (3.052-6.748)	

*p < 0.0001; M = male, F = female, HTN = hypertension, DM = diabetes mellitus, Dyslip = dyslipidemia, FH = family history, SMK = smoking, CAD = coronary artery disease

explanation for this finding could be the referral bias and subjecting more patients with DM and HTN (mixed population with or without symptoms for ischemia) for MPIs studies. Regarding asymptomatic diabetics, various prospective studies have shown a lower (6–22%) prevalence of ischemia [13]. However, we have not segregated patients with or without ischemic symptoms and this is a limitation of the study. Another limitation of this study is lack of follow up of patients especially those with normal MPIs to find out NPV. The result of this study should be read carefully, as marginal but significant rise in normal MPI over a period 8.5 years has been associated with significantly higher trends of vasodilators stress which has lower NPV than exercise. We envisaged following these cases to ascertain the NPV of normal MPIs which will be shared in future.

We conclude that over the past 8.5 years, a marginal but significant decline in abnormal and a rise in normal MPIs trend have been observed. An exorbitant rise in use of vasodilator as method of stress has also been observed. We envisaged a follow-up study to ascertain lower NPV of vasodilator as a possible reason and till than results of this and other such studies must be read cautiously.

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