کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Clinical value and severity of myocardial perfusion defects in asymptomatic diabetic patients with negative or weakly positive exercise treadmill test

Seyed Rasoul Zakavi1, Mehdi Taherpour2, Zohreh Moossavi1, Ramin Sadeghi1, Vahidreza Dabbagh Kakhki1, Haleh Rokni3

1 Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
2 Cardiology Department, Razavi Hospital, Mashhad, Iran
3 Endocrinology and Metabolism Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Article type: Original Article

ABSTRACT

Objective: Although coronary artery disease (CAD) is the leading cause of death in type 2 diabetic patients, it is frequently asymptomatic. Myocardial perfusion imaging (MPI) is reported to show ischemia in a significant number of asymptomatic diabetic patients. We studied the prevalence and severity of myocardial perfusion defects in asymptomatic diabetic patients and its clinical impact.

Methods and patients: One hundred thirty consecutive asymptomatic patients, aged 35-65 years with type 2 diabetes mellitus and with no history of CAD and no cardiac symptoms were recruited in the study. Echocardiography, electrocardiography (ECG), routine laboratory tests and exercise treadmill test (ETT) were performed and patients with weakly positive or negative ETT underwent Dipyridamole MPI. Patients with positive ETT were referred to coronary angiography. Patients were followed for at least 17 months (mean 21.7 months) and any cardiac event was recorded.

Results: We studied 81 female and 49 male patients with mean age of 51.8 years. Negative, weakly positive and positive ETT result was noted in 74.3%, 15% and 10.7% respectively. 75% of patients with positive ETT had coronary artery disease in angiography. Gated myocardial perfusion SPECT was done in 106 patients. MPI showed reversible defect in 26.9% of the patients with a mean summed stress score of 3.3±1.8. Follow up completed in 112 patients and only one patient with abnormal MPI underwent PTCA. No cardiac death, MI, UA or hospital admission occurred among our patients during follow up (17-26 months). Mean stress end diastolic volume (EDV) was significantly higher in patients with reversible defect compared to patients without reversible defect based on MPI findings (62.0±31.6 vs 48.5±18.4 ml, P=0.04). Blood glucose and HbA1c were significantly higher in patients with ischemia compared to patients without ischemia (P<0.05). Meanwhile the ratio of TG to HDL was 6.06±3.2 in ischemic patients compared to 4.8±2.3 in normal subjects (P=0.03).

Conclusion: Reversible defects are commonly seen in myocardial perfusion SPECT in asymptomatic diabetic patients and are mild in severity and not associated with adverse cardiac events. Routine approach for detection of CAD beginning with ETT seems to be appropriate in these patients.

Introduction

Prevalence of Diabetes is increasing all over the world (1). It is estimated that more than 366 million people will have diabetes in year 2030 worldwide(1). The most common cause of death in type 2 diabetes patients is coronary artery disease(2). Coronary artery disease (CAD) is often asymptomatic in these patients until the onset of myocardial infarction or sudden cardiac death (3). Ap-
proach to detection of CAD is not uniform among physi-
cians and multiple diagnostic techniques are suggested
for this purpose including myocardial perfusion imaging
(MPI), Exercise treadmill test (ETT), CT coronary angiogra-
phy (CTCA), calcium scoring and stress echocardiogra-
phy(4-7). Many studies showed silent ischemia in a sig-
nificant number of asymptomatic diabetic patients(7-9).
However the significance of detected ischemia in asym-
ptomatic patients is not well known(9-11). Different guide-
lines suggested different approaches to detection of
ischemia in diabetic patients(12-15). These guidelines are
mainly based on the consensus opinion in the absence of
valid clinical evidence. There is also a lot of controversy
regarding treatment of asymptomatic diabetic patients
with ischemia detected by MPI(16-17). We studied asym-
ptomatic diabetic patients using echocardiography, ETT
and myocardial perfusion scintigraphy. We used routine
approach for detection of ischemia beginning with ETT
and proceeding to coronary angiography in case of posi-
tive ETT result. The remaining patients with negative or
weakly positive ETT results may benefit from myocardial
perfusion SPECT. In this study the prevalence of ischemia
by MPI and its clinical impact in asymptomatic diabetic
patients with negative or weakly positive ETT is explored.

Methods and materials

We studied 130 consecutive patients with diabetes type
2 referred to endocrine clinic of Emam Reza Hospital.
All patients aged 35-65 years with no history of coronary
artery disease and no cardiac symptoms were recruited
in the study. A written consent was signed by every indi-
vidual who entered the study. A questionnaire was filled
including patients demographic information and labora-
tory tests. Exclusion criteria were pregnancy, Q wave
in electrocardiography (ECG), cardiomyopathy, cerebro-
vascular accident (CVA), or intermittent claudication,
typical chest pain or chest pain equivalent, and history
of myocardial infarction or coronary angioplasty. Labo-
ralory tests including fasting blood sugar (FBS), 2hrs post-
prandial glucose, HbA1C, lipid profile and high sensitivity
C reactive protein (hsCRP) were done in all patients. Then
patients were referred to a cardiologist for echocardiogra-
phy and exercise treadmill test. The exclusion criteria for
ETT were diabetic foot, left bundle branch block (LBBB),
proliferative retinopathy, severe degenerative knee joint
disease and chronic kidney disease (CKD). If ETT was posi-
tive or strongly positive then coronary angiography was
suggested to the patients. Otherwise patients were re-
ferred for gated myocardial perfusion SPECT (MPI). ETT
was considered as weakly positive if there was horizontal
or down sloped ST segment depression of 1-2 mm or up
sloped ST depression of greater than 1.5 mm. It is consid-
ered as positive if ST segment depression was 2-3 mm and
strongly positive if any of the followings was noted: ST
segment depression > 3 mm anytime during exercise, > 1
mm during first stage of exercise, typical chest pain dur-
ing stage 1, ST segment elevation, significant ventricular
arrhythmia (3 or more consecutive PVCs), > 10 mmHg
decrease in blood pressure. All ST segment changes were
measured 80msec after J point in most reliable leads in-
cluding V3-V6 and inferior leads.

Also patients who did not meet ETT inclusion criteria
were studied by gated MPI. Dipyridamole gated myocard-
deral perfusion SPECT was done in 106 patients using two
day protocol. Dipyridamole was infused with a dose of
0.568mg/kg of body weight over 4 minutes and 740MBq
of 99mTc-MIBI was injected 2 minutes later. A dual head
gamma camera (e-cam Siemens) was used for acquisi-
tion. All patients were imaged in supine position in a 180
degree arch from right anterior oblique (RAO45) to left
posterior oblique (LPO45). If decreased uptake was noted
in inferior wall in supine SPECT, imaging was repeated in
prone position to exclude diaphragmatic attenuation.
The images were reviewed by two experienced nuclear
medicine specialist and consensus opinion was consid-
ered for interpretation. If consensus was not achieved,
the opinion of the third nuclear medicine specialist was
used for conclusion. Any reversible defect was considered
abnormal. Any defect in inferior wall with improvement
in prone images as well as any mild fixed anterior wall
defect in women with normal wall motion was consid-
ered normal. Also semiquantification was done using
a 17 segment model and 5 points grading score. In this
system, the myocardium is reviewed in 16 short axis seg-
ments and one long axis segment. Normal uptake in each
segment scored 0, mild decreased uptake 1, moderate de-
creased uptake 2, severe decreased uptake 3 and absent
uptake scored 4. QPS software (Cedars-Sinai medical cen-
ter, LA, USA) was used for semiquantification and com-
parison with normal data pool.

Patients with ischemia or infarction in myocardial
SPECT as well as patients with coronary stenosis on an-
giography were referred to cardiologist for appropriate
therapy. All patients in our study were treated during
the follow up according to the AHA/ACC guidelines(14).
Patients were followed every 6 months for at least 17
months and any cardiac event, admission to cardiac unit,
angioplasty or cardiac surgery was recorded. The project
was approved by a local ethical committee.

Univariate analysis was done for description of the data.
Statistical analysis was performed using SPSS software
(SPSS, V 11.5) to compare different variables in patients
with and without ischemia using independent t-test and
chi-square tests. P value of <0.05 was considered signifi-
cant in all comparisons.

Results

One hundred and thirty patients (81 female, 49 male)
with mean age of 51.8 ± 7.3 years enrolled in the study. The mean duration of diabetes since diagnosis was 7.8 ± 3.3 years. The mean body mass index (BMI) was 27.9±13.8 kg/m². Table 1 shows demographic and laboratory findings in our patients. Echocardiography was done in all patients by a single instrument (Vivid 3, GE, Norway). The echo findings showed mean LV ejection fraction of 61.9±5.7%. Left ventricular motion abnormality was noted in 31% and left ventricular hypertrophy was seen in 55 patients (43%). Rest ECG showed mild ST depression or T inversion in 14 patients (10.8%).

Table 1. Demographic and Laboratory information of patients.

| Variable                  | Mean ± SD   |
|---------------------------|-------------|
| Age (years)               | 51.8±7.3    |
| SEX (M/F)                 | 1.6         |
| Waist circumference (cm)  | 94.9±9.2    |
| FBS (mg/dl)               | 170.3±66.8  |
| 2hrs PPBS (mg/dl)         | 230±64.9    |
| Hba1C (%)                 | 8±±2.2      |
| Total Cholesterol (mg/dl) | 209±43.9    |
| Triglyceride (mg/dl)      | 188.9±73.5  |
| HDL-C (mg/dl)             | 39.0±7.4    |
| LDL-C (mg/dl)             | 132.7±37.1  |
| HsCRP (ng/dl)             | 2.6±4.2     |

ETT was done in one hundred and thirteen patients of which 74.3% were negative, 15% were weakly positive, 1.8% were positive, and 8.9% were strongly positive. Maximum Heart Rate (MHR) was defined as 220 minus age and all patients undergoing ETT reached at least 85% of MHR. Of 130 patients, 10 patients didn’t agree to undergo myocardial perfusion imaging. Twelve patients had positive or strongly positive ETT and were directly referred to coronary angiography. Gated myocardial perfusion SPECT was done in 106 patients. In 2 patients nongated imaging was done due to rhythm irregularities. Seventy nine patients (73.1%) had normal MPI, while 29 patients (26.9%) had reversible defects. No fixed defect was noted in our patient. Mean (±SD) summed stress score was 3.3 ± 1.8 and mean (SD) summed rest score was 0.72 ± 0.75 in patients with reversible defect. Mean (SD) stress end diastolic volume (EDV) was significantly higher in patients with reversible defect compared to patients without reversible defect based on MPI findings (62.0±3.16 Vs 48.5±18.4 ml, P=0.044). Interestingly the rest EDV was higher too in patients with reversible defects, however it did not reach statistical significance (P=0.07).

Angiography was recommended for 12 patients after a positive or strongly positive ETT and was performed in 4 patients. One patient had 3 vessel disease and underwent coronary artery bypass grafting (CABG). Another patient had single vessel disease and underwent balloon angioplasty and a drug eluting stent was placed in the LAD. One patient had severe 3VD and did not accept CABG and is under medical treatment with no cardiac event up to 24 months. The 4th patient who underwent coronary angiography had a 50% stenosis in LAD and is being treated with medical therapy.

Patients were visited every 6 months and any cardiac event was recorded. Also patients were called to come for review of data and visit if they were not visited in due time. One hundred and thirteen patients (86.9%) completed follow up. Patients were followed for at least 17 months and mean time of follow up was 21.7±1.7 months. During follow up 1 patient with abnormal MPI underwent coronary angiography followed by PTCA. No cardiac death, myocardial infarction (MI), unstable angina (UA) or cardiac admission was occurred among our patients.

Mean age of patients with and without reversible defect was 51.95±7.3 and 51.97±7.0 years respectively. The mean follow up time was not significantly different between patients with normal MPI (22.1±1.7 months) and patients with reversible defect (21.2±1.1 months).

Blood glucose and HbA1c were significantly higher in patients with ischemia compared to patients without ischemia (P<0.05). However there was no significant difference in total cholesterol, HDL-C and LDL-C.

Table 2. Comparison of laboratory findings in patients with and without reversible defect in MPI.

| Variable                  | Normal MPI | Reversible defect | P value |
|---------------------------|------------|-------------------|---------|
| Number of patients        | 79         | 29                |         |
| Age (years)               | 51.9±7.3   | 51.9±7.0          | 0.99    |
| Waist circumference (cm)  | 95.9±8.3   | 93.2±10.4         | 0.16    |
| FBS (mg/dl)               | 165±43.0   | 190±46.5          | 0.01    |
| 2hrs PPBS (mg/dl)         | 237.8±68.1 | 242.9±59.5        | 0.72    |
| HbA1C (%)                 | 8.4±1.9    | 9.4±2.3           | 0.02    |
| Total Cholesterol (mg/dl) | 205.8±45.7 | 216±41.1          | 0.30    |
| Triglyceride (mg/dl)      | 180.4±67.8 | 208.2±82.0        | 0.08    |
| HDL-C (mg/dl)             | 39.3±7.6   | 36.8±7.2          | 0.12    |
| LDL-C (mg/dl)             | 130.9±39.8 | 138.7±32.3        | 0.35    |
| HsCRP (ng/dl)             | 2.6±3.6    | 2.9±5.8           | 0.68    |
| TG/HDL                    | 4.8±2.3    | 6.0±4.2           | 0.03    |
| BMI                       | 27.9±4.0   | 27.8±3.8          | 0.96    |
| Waist Height Ratio        | 0.59±0.06  | 0.58±0.07         | 0.31    |
triglyceride (TG) or HsCRP level in patients with ischemia compared to patients without ischemia (Table 2). Meanwhile the ratio of TG to HDL was 6.06±3.2 in ischemic patients compared to 4.8±2.3 in normal subjects (P=0.03).

Waist circumference, BMI and waist to height ratio (WHR) were not significantly different between patients with and without ischemia in myocardial perfusion SPECT (P=0.3).

Using chi-square test, prevalence of risk factors was compared in patients with and without reversible defects (Table 3). There was no significant difference in prevalence of hypertension, hyperlipidemia, smoking, family History of CAD, microalbuminuria, retinopathy or foot ulcer in patients with and without reversible defect (P>0.05).

| Variable                  | Normal MPI (%) | Reversible defect (%) | P value |
|---------------------------|----------------|-----------------------|---------|
| Hypertension              | 52.6           | 32.1                  | 0.08    |
| Hyperlipidemia            | 74.7           | 78.6                  | 0.80    |
| Smoking                   | 3.8            | 0.0                   | 0.56    |
| Retinopathy               | 34.6           | 39.3                  | 0.65    |
| Microalbuminuria          | 35.9           | 46.4                  | 0.37    |
| LVH (echocardiography)    | 39.7           | 46.4                  | 0.65    |
| Stress EDV (ml)           | 48.5±18.3      | 60.8±28.4             | 0.04    |

Discussion

More than 200 million people in the world suffer from diabetes and 65%-85% of these patients finally die from CAD(1). Myocardial infarction and sudden cardiac death are common presentation of CAD in diabetic patients(3). Also the number of patients with diabetes mellitus was increasing among patients admitted to the hospital with myocardial infarction(16). In addition diabetic patients with abnormal SPECT of abnormal stress echocardiography had worse prognosis than nondiabetic patients(19). So many researchers tried to detect silent ischemia in asymptomatic diabetic patients in order to prevent future cardiac events(7-8, 10, 20-22). Variable modalities are used for detection of CAD in asymptomatic diabetic patients with different success rates. These techniques include CT-Angiography and calcium scoring, MPI, stress echocardiography and ETT(4-7, 23-24). However the clinical benefit of screening of these patients remains to be proved(4).

We used a routine approach for detection of CAD using ETT first. Our study showed that 10.7% of patients had positive or strongly positive ETT. From these patients who accepted coronary angiography 75% had significant CAD and 25% had borderline stenosis of about 50% in coronary arteries.

Also reversible myocardial perfusion defect was observed in 29 patients (26.9%). This is similar to the findings by DIAD study which reported 22% of ischemia among asymptomatic patients (7). In DIAD study the age range was 50-75 years while our study had a wider range of age(7). Sozzi et al. found 28% prevalence of ischemia in a group of asymptomatic diabetic patients who had a mean age of 62 years (24). A recent study showed a prevalence of 25% of ischemia in MPI in asymptomatic diabetic patients with mean age of 53±10 years (25). Similar findings in these studies may suggest age independence of prevalence of silent ischemia in diabetic patients.

From 29 patients with silent ischemia in our study only one patient (3.2%) underwent PTCA during follow up. No other minor or major cardiac event was noted in this group. Young et al. also reported PPV of 6% for reversible defects in predicting MI or cardiac death during a mean follow up of 4.8 years in asymptomatic patients with diabetes(2). In a randomized trial they noted that use of MPI had no discernable effect on subsequent cardiac events(2).

In our study mean summed stress score was 3.3±1.8 in patients with reversible defect suggesting that most of these patients had minimal ischemia. Our study also showed that only 2.7% of asymptomatic diabetic patients had defects involving more than 10% of the left ventricle. In DIAD study the large defect (≥10%) was reported in only 1% of population. It is reported that the larger the MPI defect in asymptomatic diabetic patients, the greater the incidence of cardiac events(2). Also in asymptomatic patients (not all diabetics) MPI ischemia of ≥7.5% (using 20 segment analysis) was considered as independent predictor of future events(11). The severity and extent of the ischemia as determined by SSS is not extensively studied in asymptomatic diabetic patients. Our study showed that MPI defects in asymptomatic diabetic patients is mainly small in magnitude (as assessed by SSS) and does not result in adverse cardiac events.

Functional indices of the LV using MPI have been studied in asymptomatic diabetic patients(26). In one study 16.7% of patients had low LV ejection fraction (LVEF) which was associated with older age and higher annual mortality rate (26). No patient in our study had LVEF of less than 45% in gated myocardial perfusion SPECT. However mean post stress EDV was significantly higher in patients with reversible defects compared to patients without reversible defects. Also left ventricular hypertrophy was seen in 43% of our patients. Left ventricular hypertrophy is reported to be higher among diabetic patients compared to nondiabetic subjects(27). Bertoni et al. in a study of nearly 5000 diabetic patients by MRI found significant ethnic-specific differences in LV mass as well as EDV and concluded that these findings are not related to the subclinical CAD(27).

In our study FBS and HbA1c level was higher in patients...
Clinical Value of MPI in diabetics

with ischemia confirming that ischemia is more frequent in poorly controlled patients. It is also reported that higher glucose level in these patients may be associated with higher complications(3). However we could not find any difference in other laboratory variables like total, HDL and LDL cholesterol, triglyceride, HsCRP and 2hrs postprandial blood glucose level between patients with and without ischemia.

Bittner et al(28) reported that the ratio of TG/HDL is a powerful independent predictor of all cause mortality and cardiovascular events in women. In our study TG/HDL ratio was significantly higher in patients with ischemia compared to normal subjects.

Tseng in a study of diabetic patients found that among obesity factors of BMI, waist circumference, waist to hip ratio and waist to height ratio, the waist to height ratio had the greatest magnitude of odds ratio between patients with and without CAD(29). However others could not find significant difference in obesity indices and coronary artery calcifications(30). Also it is shown that intima-media thickness of the carotid is not significantly different in patients with and without central obesity(31). We also could not find any difference in BMI, waist circumference and waist to height ratio between patients with and without ischemia.

As intensive cardiac risk factor modification is recommended in all patients with type 2 diabetes, the role of screening tools for detection of mild ischemia is also questioned(32). Routine use of MPI or stress echocardiography in asymptomatic diabetic patients as well as its cost-effectiveness is challenged by many authors(33-36). MPI may detect clinically nonsignificant ischemia in these patients and may not change the clinical decision(2, 35). However, if MPI findings showed high risk pattern, the patients get a survival advantage by undergoing CAGB(37). No survival advantage was noted in treating patients with low to intermediate risk MPI patterns(37). In this study we found that MPI defects are mainly small in magnitude in asymptomatic diabetic patients with negative or weakly positive ETT.

Our study had a limitation of relatively low number of patients. Longer follow up in a large number of patients and analysis in different subgroups as well as cost-effectiveness analysis will help in defining the best approach to CAD detection in asymptomatic diabetic patients.

Conclusion

Our study showed that although myocardial perfusion defects were frequently seen in asymptomatic diabetic patients, defects were of small magnitude and did not reflect adverse outcome. Routine MPI imaging in all asymptomatic diabetic patients is not recommended. Routine approach to CAD beginning with ETT may be more justifiable in asymptomatic diabetic patients.

Acknowledgement

This study was supported by a research from the Mashhad University of Medical Sciences.

References:

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004 May;27(5):1047-53.
2. Young LH, Wackers FJ, Chyun DA, Davie JA, Barrett EJ, Taillefer R, et al. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. Jama. 2009 Apr 15;301(15):1547-55.
3. Jouven X, Lemaiitre RN, Rea TD, Sotoodehnia N, Empaha J, Siscovick DS. Diabetes, glucose level, and risk of sudden cardiac death. Eur Heart J. 2005 Oct;26(20):2442-7.
4. Bax JJ, Young LH, Frye ER, Bonow RO, Steinberg HO, Barrett EJ. Screening for coronary artery disease in patients with diabetes. Diabetes Care. 2007 Oct;30(10):2279-86.
5. Fateh-Moghadam S, Reuter T, Himm P, Plockinger U, Dietz R, Bockisch W. Stress echocardiography for risk stratification of asymptomatic patients with type 2 diabetes mellitus. Int J Cardiol. 2009 Jan 1;131(1):284-90.
6. Scholte AJ, Schuijf JD, Karagiatisseng AC, Jukema JW, Pundziute G, van der Wall EE, et al. Prevalence of coronary artery disease and plaque morphology assessed by multi-slice computed tomography coronary angiography and calcium scoring in asymptomatic patients with type 2 diabetes. Heart. 2008 Mar;94(5):290-5.
7. Wackers FJ, Young LH, Inzucchi SE, Chyun DA, Davie JA, Barrett EJ, et al. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. Diabetes Care. 2004 Aug;27(8):1954-61.
8. Bax JJ, Bonow RO, Tischele D, Inzucchi SE, Barrett EJ. The potential of myocardial perfusion scintigraphy for risk stratification of asymptomatic patients with type 2 diabetes. J Am Coll Cardiol. 2006 Aug 15;48(4):754-60.
9. Feringa HH, Karagiannis SE, Vidicikov R, Elbenhdy A, ten Cate FJ, Noordzij PG, et al. The prevalence and prognosis of unrecognized myocardial infarction and silent myocardial ischemia in patients undergoing major vascular surgery. Coron Artery Dis. 2007 Nov;18(7):571-6.
10. Zellweger MJ, Hachamovitch R, Kang X, Hayes SW, Friedman JD, Germano G, et al. Prognostic relevance of symptoms versus objective evidence of coronary artery disease in diabetic patients. Eur Heart J. 2004 Apr;25(7):543-50.
11. Zellweger MJ, Hachamovitch R, Kang X, Hayes SW, Friedman JD, Germano G, et al. Threshold, incidence, and predictors of prognostically high-risk silent ischemia in asymptomatic patients without prior diagnosis of coronary artery disease. J Nucl Cardiol. 2009 Mar;16(2):193-200.
12. Hurmi CA, Perret S, Monkbaron D, Gaillard R, Ruiz J. Coronary artery disease screening in diabetic patients: how good is guideline adherence? Swiss Med Wkly. 2007 Apr 7;137(13-14):199-204.
13. Ryden L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, de Boer MJ, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur Heart J. 2007 Jan;28(1):88-136.
14. Smith SC, Jr., Allen J, Blair SN, Bonow RO, Brass LM, Fonarow GC, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. Circulation. 2006 May 16;113(20):2363-72.
15. Valensi P. [Silent coronary artery disease in diabetic patients]. New guidelines]. Rev Med Liege. 2005 May-Jun;60(5-6):315-8.
16. Beishuizen ED, Jukema JW, Tamsma JT, van de Ree MA, van der Vlijer JC, Putter H, et al. No effect of statin therapy on silent myocar-
cardiac ischemia in patients with type 2 diabetes without manifest cardiovascular disease. Diabetes Care. 2005 Jul;28(7):1675-9.
17. Almada FQ, Rason TT, Nathan S, Kavinsky CJ. Silent myocardial ischemia: concepts and controversies. Am J Med. 2004 Jan 15;106(1):72-8.
18. Rogers WJ, Frederick PD, Stoehr E, Canto G, Ornato JP, Gibson CM, et al. Trends in presenting characteristics and hospital mortality among patients with ST elevation and non-ST elevation myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J. 2008 Dec;156(6):1026-34.
19. Cortigiani L, Bigi R, Scarci R, Landi P, Bovenzi F, Picano E. prognostic value of pharmacological stress echocardiography in diabetic and nondiabetic patients with known or suspected coronary artery disease. J Am Coll Cardiol. 2006 Feb 7;47(3):605-10.
20. Prior JO, Monbaron D, Koehli M, Calcagno ML, Ruiz J, Bischof Delaloye A. Prevalence of symptomatic and silent stress-induced perfusion defects in diabetic patients with suspected coronary artery disease referred for myocardial perfusion scintigraphy. Eur J Nucl Med Mol Imaging. 2005 Jan;32(1):59-69.
21. Smario PE, Carvalho AC, Teixeira AS, Thom A, Rodrigues F, Nengetheo R, et al. Coronary artery disease in asymptomatic type-2 diabetic women. A comparative study between exercise test, cardiopulmonary exercise test, and dipyridamole myocardial perfusion scintigraphy in the identification of ischemia. Arq Bras Cardiol. 2007 Nov;89(3):263-9, 90-7.
22. Choi JK, Koo BK, Kim HS, Cho YM, Kang HJ, Cho YE, et al. Prognostic significance of asymptomatic coronary artery disease in patients with diabetes and need for early revascularization therapy. Diabet Med. 2007 Sep;24(9):1003-11.
23. Barthelemy O, Le Feuvre C, Timsit J. Silent myocardial ischemia screening in patients with diabetes mellitus. Arq Bras Endocrinol Metabol. 2007 Mar;51(2):285-93.
24. Sozzi FB, Elhendy A, Rizzello V, Biagini E, van Domburg RT, Schinol Metabol. 2007 Mar;51(2):285-93.
25. Sozzi FB, Elhendy A, Rizzello V, Biagini E, van Domburg RT, Schinol Metabol. 2007 Mar;51(2):285-93.
26. Chareonthaitawee P, Sorajja P, Rajagopalan N, Miller TD, Hodge DO, Frye RL, et al. Prevalence and prognosis of left ventricular systolic dysfunction in asymptomatic diabetic patients with unknown coronary artery disease referred for stress single-photon emission computed tomography and assessment of left ventricular function. Am Heart J. 2007 Sep;154(3):567-74.
27. Bertoni AG, Golf DC, Jr., D’Agostino RB, Jr., Liu K, Hundley WG, Lima JA, et al. Diabetic cardiomyopathy and subclinical cardiovascular disease: the Multi-Ethnic Study of Atherosclerosis (MESA). Diabetes Care. 2006 Mar;29(3):588-94.
28. Bittner V, Johnson BD, Zineh I, Rogers WJ, Vido D, Marroquin OC, et al. The triglyceride/high-density lipoprotein cholesterol ratio predicts all-cause mortality in women with suspected myocardial ischemia: a report from the Women’s Ischemia Syndrome Evaluation (WISE). Am Heart J. 2009 Mar;157(3):548-55.
29. Tseng CH. Waist-to-height ratio and coronary artery disease in Taiwanese type 2 diabetic patients. Obesity (Silver Spring). 2008 Dec;16(12):2754-9.
30. Conway B, Miller RG, Costacou T, Fried L, Kelsey S, Evans RW, et al. Double-edged relationship between adiposity and coronary artery calcification in type 1 diabetes. Diab Vasc Dis Res. 2007 Dec;4(4):332-9.
31. Yasuda T, Matsuhashi M, Fujiki N, Sakamoto F, Tsuji M, Fujisawa N, et al. Is central obesity a good predictor of carotid atherosclerosis in Japanese type 2 diabetes with metabolic syndrome? Endocr J. 2007 Dec;54(5):695-702.
32. Rutter MK NR. The changing costs and benefits of screening for asymptomatic coronary heart disease in patients with diabetes. Nat Clin Pract Endocrinol Metab. 2007;3(1):26-35.
33. Miller TD, Redberg RF, Wackers FJ. Screening asymptomatic diabetic patients for coronary artery disease: why not? J Am Coll Cardiol. 2006 Aug 15;48(4):761-4.
34. Hayashino Y, Shimbo T, Tsuji S, Ishii H, Kondo H, Nakamura T, et al. Cost-effectiveness of coronary artery disease screening in asymptomatic patients with type 2 diabetes and other atherogenic risk factors in Japan: factors influencing on international application of evidence-based guidelines. Int J Cardiol. 2007 May 16;118(1):88-96.
35. Scognamiglio R, Negut C, Ramondo A, Tiengo A, Avogaro A. Detection of coronary artery disease in asymptomatic patients with type 2 diabetes mellitus. J Am Coll Cardiol. 2006 Jan 3;47(1):55-71.
36. Rakhot DJ, Downey M, Jeffries I, Moir S, Prins JB, Marwick TH. Screening for coronary artery disease in patients with diabetes: a Bayesian strategy of clinical risk evaluation and exercise echocardiography. Am Heart J. 2005 Nov;150(5):1074-80.
37. Sorajja P, Chareonthaitawee P, Rajagopalan N, Miller TD, Frye RL, Hodge DO, et al. Improved survival in asymptomatic diabetic patients with high-risk SPECT imaging treated with coronary artery bypass grafting. Circulation. 2005 Aug 10;112(5 Suppl)I:II-6.
کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله