DIABETES RESEARCH AND CLINICAL PRACTICE 107 (2015) 267–272

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Clinical characteristics and course of patients with diabetes entering cardiac rehabilitation

Francesco Giallauria [a,*], *Francesco Fattirolli* [b], *Roberto Tramarin* [c], *Marco Ambrosetti* [d], *Raffaele Griffo* [e], *Carmine Riccio* [f], *Stefania De Feo* [g], *Massimo Francesco Piepoli* [h], *Carlo Vigorito* [a], *on behalf of the ISYDE-2008 Investigators of the Italian Association for Cardiovascular Prevention, Rehabilitation (GICR-IACPR)*

[a] Department of Translational Medical Sciences, Division of Internal Medicine and Cardiac Rehabilitation, University of Naples ''Federico II'', Naples, Italy
[b] Department of Critical Care Medicine and Surgery, Cardiac Rehabilitation Unit, University of Florence and Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy
[c] Cardiac Rehabilitation Unit, IRCCS Policlinico San Donato, Italy
[d] Cardiovascular Rehabilitation Unit, Le Terrazze Clinic, Cunardo, Italy
[e] Cardiac Rehabilitation Unit, Department of Cardiology, La Colletta Hospital, Arenzano, Italy
[f] Cardiac Rehabilitation, Azienda Ospedaliera S. Anna e S. Sebastiano di Caserta, Italy
[g] Cardiology Unit, Dr Pederzoli Clinic, Peschiera del Garda, Italy
[h] Heart Failure Unit, Cardiology, G. da Saliceto Hospital, Piacenza, Italy

ARTICLE INFO

Article history:
Received 29 May 2014
Received in revised form 20 September 2014
Accepted 24 November 2014
Available online 3 December 2014

Keywords:
Cardiac rehabilitation
Diabetes
Exercise training
Myocardial infarction
Chronic heart failure
Cardiopulmonary exercise testing

ABSTRACT

Background: Using data from the Italian SurveY on carDiac rEhabilitation (ISYDE-2008), this study provides insight into the level of implementation of Cardiac Rehabilitation (CR) in patients with diabetes.

Methods: Data from 165 CR units were collected online from January 28th to February 10th, 2008.

Results: The study cohort consisted of 2281 patients (66.9 ± 12 yrs); 475 (69.7 ± 10 yrs, 74% male) patients with diabetes and 1806 (66.2 ± 12 yrs, 72% male) non-diabetic patients. Compared to non-diabetic patients, patients with diabetes were older and showed more comorbidity [myocardial infarction (32% *vs.* 19%, $p < 0.0001$), peripheral artery disease (10% *vs.* 5%, $p < 0.0001$), chronic obstructive pulmonary disease (20% *vs.* 11%, $p < 0.0001$), chronic kidney disease (20% *vs.* 6%, $p < 0.0001$), and cognitive impairment (5% *vs.* 2%, $p = 0.0009$), respectively], and complications during CR [re-infarction (3% *vs.* 1%, $p = 0.04$), acute renal failure (9% *vs.* 4%, $p < 0.0001$), sternal revision (3% *vs.* 1%, $p = 0.01$), inotropic support/mechanical assistance (7% *vs.* 4%, $p = 0.01$), respectively]; a more complex clinical course and interventions with less functional evaluation and a different pattern of drug therapy at hospital discharge. Notably, in 51 (3%) and in 104 (6%) of the non-diabetic cohort, insulin and hypoglycemic agents were prescribed, respectively, at hospital discharge from CR suggesting a careful evaluation of the glycemic metabolism during CR program, independent of the

* *Corresponding author at*: Department of Translational Medical Sciences, Cardiac Rehabilitation Unit, University of Naples ''Federico II'', via S. Pansini 5, 80131 Naples, Italy. Tel.: +39 081 7462639; fax: +39 081 7462639.
E-mail address: giallauria@libero.it (F. Giallauria).
http://dx.doi.org/10.1016/j.diabres.2014.11.006

diagnosis at the admission. Mortality was similar among diabetic compared to non-diabetic patients (1% *vs.* 0.5%, $p = 0.23$).

Conclusions: This survey provided a detailed overview of the clinical characteristics, complexity and more severe clinical course of diabetic patients admitted to CR.

1. Introduction

Mounting evidence suggests that exercise training alone or as core component of cardiac rehabilitation (CR) programs has several beneficial effects reducing mortality [1], preventing cardiac remodeling [2,3], and improving cardiovascular functional capacity and myocardial perfusion [4–7]. The improvement of endothelial function [8], the anti-inflammatory properties [9,10], the improvement of neurohormonal and autonomic balance [11–15], and the reduction of oxidative stress [16] might be some of the putative mechanisms by which exercise training exerts its beneficial effects.

Some of the beneficial effects of exercise-based CR observed in the general population of coronary heart disease (CHD) patients have also been reported in patients with diabetes [17,18]. However to the best of our knowledge, there are no data that specifically describe in large population the prevalence of diabetes in patients undergoing CR programs, and their clinical characteristics and course during the CR program. Therefore, the present survey aimed at providing an insight in the clinical characteristics and course of a diabetic population in the real world of CR in Italy.

2. Methods

2.1. Study design

The multicenter, prospective observational study design of the ISYDE-2008 has been described in detail elsewhere [19–21]. Briefly, the primary purpose of the study was to explore the current organization, settings and provision of CR in Italy and to describe the patient population referred to CR, giving a comprehensive and detailed description of clinical characteristics, risk profile, diagnostic procedures, exercise and educational program, discharge modalities, treatment at discharge and follow-up schedules. The enrolment period lasted from January 28th to February 10th 2008. Patients were referred to CR at hospital discharge after the index event and then the data relate to those patients who were discharged from CR in the 2 week period. Data were collected on a web-based Case Report Form, which reported data of all the consecutive patients discharged from CR programs in the 2-week study period. The present study focused on patients with diabetes ($n = 160$ (34%) with type 1 diabetes and $n = 315$ (66%) type 2 diabetes). As a part of geriatric multidimensional evaluation, performed in about one fourth of our population, cognitive function was evaluated by MMSE [22], and cognitive impairment was assigned when corrected MMSE value was <21.

2.2. Participating centers

All Italian residential and outpatient CR centers were invited to participate on a purely voluntary basis by the executive board of the study and by the regional GICR-IACPR coordinator, who was responsible for interfacing with the investigators in each of the participating centers and oversaw the implementation of the survey protocol. Data collected in the study refer to 165 CR units (87% of all invited facilities). The complete list of ISYDE-2008 investigators and participating Centers with names of the director or contact physician is reported in Appendix 1.

2.3. Role of the funding source

No funding sources had any role in the study design, conduct, data collection, analysis, data interpretation, or writing of this report. The GICR-IACPR coordinated the study, managed the data, and undertook all analyses. All members of the scientific board and writing committees had full access to the database and assumed final responsibility for the results submitted for publication.

2.4. Statistical analysis

The main analysis was performed subdividing the study cohort into two groups, according to the diagnosis of diabetes. Data are expressed as means ± standard deviation (SD) or proportions. Comparisons between groups were performed by unpaired *t*-test, χ^2 or Fisher exact test as required. Correlations between variables were assessed with Pearson's correlation coefficient. Predictors of death (mortality during CR programs) were evaluated with multivariate logistic regression analysis. All analyses were performed using SAS (Version 9.1, Cary, NC) with significance set at $p < 0.05$.

3. Results

Table 1 summarizes the demographic characteristics of the study population. The study cohort consisted of 2281 patients (66.9 ± 12 yrs); 475 (69.7 ± 10 yrs, 74% male) patients with diabetes and 1806 (66.2 ± 12 yrs, 72% male) non-diabetic patients. Diabetic patients showed a significantly higher cardiovascular risk factors score (including smoking, history, hypertension, dyslipidemia, obesity, diabetes, sedentary lifestyle, and early menopause) compared to the non-diabetic cohort ($p < 0.0001$) (Table 1).

Compared to non-diabetic, patients with diabetes had more comorbidity such as previous percutaneous coronary intervention (PCI) and cardiac surgery, myocardial infarction,

Table 1 – Demographics characteristics of the study population (n, %).

	Diabetics ($n = 475$)	Non-diabetics ($n = 1806$)	p value
Age (years) (mean ± SD)	69.7 ± 10	66.2 ± 12	<0.0001
Gender (male)	340 (74)	1337 (72)	0.28
Cardiovascular risk factors[a]			
0–2 (low)	65 (14)	846 (47)	<0.0001
3–5 (medium)	307 (64)	852 (47)	
>5 (high)	103 (22)	108 (6)	

[a] Smoking, family history of early coronary heart disease, high blood pressure, hypercholesterolemia, body mass index >27, sedentary lifestyle, early menopause.

peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and cognitive impairment (Table 2).

During CR programs, patients with diabetes developed more complications such as acute myocardial infarction, worsening of CKD or new onset of renal failure, and required more frequently inotropic support or sternal revision after surgery compared to non-diabetic patients (Table 3).

Regarding diagnostic or therapeutic procedures, patients with diabetes underwent more venous infusion, geriatric multidimensional evaluation and individualized exercise sessions (Table 4). Echocardiography showed a lower percentage of diabetic patients with preserved left ventricular ejection fraction (LVEF > 50%) compared to non-diabetic patients (58% *vs.* 69%, $p < 0.0001$, respectively). As many as 110 patients with diabetes (23%) was unable to perform any physical performance test (6MWT, exercise stress testing or cardiopulmonary exercise testing); this proportion was significantly greater than in non-diabetic patients (20%, $p < 0.001$). Compared to non-diabetic patients not performing any physical performance testing, diabetic patients not performing any physical performance testing showed a higher percentage of comorbidity such as myocardial infarction (30% *vs.* 15%, $p = 0.0003$), heart failure (27% *vs.* 12%, $p < 0.0001$), carotid arteries atherosclerosis (12% *vs.* 5%, $p = 0.007$), PAD (13% *vs.* 5%, $p = 0.002$), COPD (23% *vs.* 13%, $p = 0.01$), CKD (38% *vs.* 9%, $p < 0.0001$), cognitive impairment (15% *vs.* 4%, $p < 0.0001$), and orthopedic disease (26% *vs.* 13%, $p = 0.0005$); and a higher percentage of complications during the CR program such as cognitive decline (11% *vs.* 2%, $p < 0.0001$), worsening of CKD or new onset of renal failure (13% *vs.* 6%, $p = 0.01$), thoracentesis (6% *vs.* 2%, $p = 0.04$), and need of inotropic support (5% *vs.* 1%, $p = 0.006$), respectively.

At discharge, compared to non-diabetics, patients with diabetes were more frequently prescribed angiotensin II receptor blockers, nitrates, diuretics, statins, aspirin, and calcium channel blockers (Table 5). No significant differences were observed in beta-blockers, omega-3 fatty acids, and digitalis or amiodarone discharge prescription among the two cohorts (Table 5). Notably, in 51 (3%) and in 104 (6%) of the non-diabetic cohort, insulin and hypoglycemic agents were prescribed, respectively, at hospital discharge from CR (Table 5). Data were also analyzed by including these 155 patients among the diabetic group without showing any significant differences in outcomes. These findings suggest a careful evaluation of the glycemic metabolism during CR program, independent of the diagnosis at admission. Mortality was similar among diabetic compared to non-diabetic patients (1% *vs.* 0.5%, $p = 0.23$).

Table 2 – Previous interventions and comorbidity (n, %).

	Diabetics ($n = 475$)	Non-diabetics ($n = 1806$)	p value
Previous percutaneous transluminal coronary angioplasty	64 (13)	161 (9)	0.003
Previous cardiac surgery	67 (14)	183 (10)	0.01
Previous myocardial infarction	154 (32)	349 (19)	<0.0001
Peripheral artery disease[a]	50 (10)	101 (5)	<0.0001
Chronic obstructive pulmonary disease	96 (20)	202 (11)	<0.0001
Chronic kidney disease	97 (20)	103 (6)	<0.0001
Cognitive impairment	24 (5)	40 (2)	0.0009

[a] Fontaine stage >1 or previous revascularization.

Table 3 – Complications during cardiac rehabilitation programs (n, %).

	Diabetics ($n = 475$)	Non-diabetics ($n = 1806$)	p value
Atrial fibrillation	92 (10)	360 (20)	0.78
Severe ventricular arrhythmias[a]	24 (5)	66 (4)	0.16
Permanent pacemaker implantation	14 (3)	56 (3)	0.86
Acute myocardial infarction (re-infarction)	12 (3)	23 (1)	0.04
Cerebrovascular events[b]	10 (2)	31 (2)	0.57
Cognitive Impairment[*]	9 (2)	29 (2)	0.66
Anemia[c]	78 (16)	235 (13)	0.06
Worsening of CKD or new onset of renal failure[d]	43 (9)	76 (4)	<0.0001
Sternal revision	13 (3)	21 (1)	0.01
Inotropic support/ mechanical assistance	34 (7)	78 (4)	0.01
Respiratory assistance[e]	27 (6)	68 (4)	0.06
Systemic infections	20 (4)	58 (3)	0.28
Death	5 (1)	10 (0.5)	0.23

[a] >30 s or symptomatic ventricular tachycardia.
[b] Stroke, transient ischemic attack.
[c] Hb ≤10 g/dl, or ≥3 g/dl reduction with respect to the pre-index event value.
[d] Creatinine increase ≥1 mg/dl.
[e] Including oxygen therapy, mechanical ventilation, continuous positive airway pressure (cPAP), bilevel positive airway pressure (biPAP) >96 h.
[*] Worsening of cognitive impairment or new onset of cognitive impairment.

4. Discussion

To the best of our knowledge, the present study is the first to explore the characteristics of the "real world" diabetic

Table 4 – Diagnostic and therapeutic procedures during cardiac rehabilitation programs (*n*, %).

	Diabetics ($n = 475$)	Non-diabetics ($n = 1806$)	*p* value
6-Minute walking test on admission	222 (47)	761 (42)	0.07
6-Minute walking test at discharge	205 (43)	742 (41)	0.41
Exercise stress testing on admission	80 (17)	366 (20)	0.09
Exercise stress testing at discharge	151 (32)	554 (30)	0.64
Cardiopulmonary exercise stress testing on admission	22 (4)	100 (5)	0.43
Cardiopulmonary exercise stress testing at discharge	37 (8)	120 (7)	0.38
Unable to perform any physical performance test	110 (23)	378 (20)	0.01
Venous infusions	76 (16)	163 (9)	<0.0001
Thoracentesis	11 (2)	21 (1)	0.06
Blood transfusions	7 (1)	15 (1)	0.20
Geriatric multidimensional evaluation	123 (26)	331 (18)	0.0002
Computed tomography	28 (6)	61 (3)	0.01
Individual exercise sessions	149 (31)	438 (24)	0.002

patients admitted to CR programs in Italy. The major findings of this study were the higher burden of cardiovascular risk factors and comorbidities associated with a worse clinical course during CR in patients with diabetes compared to non-diabetic patients.

This survey showed a higher prevalence of diabetic patients with previous PCI or coronary artery bypass graft (CABG) participating to CR programs. Patients with diabetes undergoing myocardial revascularization have worse survival than other CAD patients [23–26]. Several studies have reported that PCI in patients with diabetes may be associated with poor long-term results [27,28]. Yu et al. [29], in a cohort of 418 patients with CAD, reported that diabetes was associated to higher mortality in patients with myocardial infarction or revascularization who underwent CR ($\chi^2 = 21.9$, $p < 0.0001$). Moreover, the presence of diabetes independently predicted rehospitalization ($\chi^2 = 4.8$, $p = 0.03$). In a large retrospective analysis of patients undergoing elective PCI with balloon angioplasty or/and bare-metal stent implantation, diabetes was found to have a negative prognostic impact on cardiovascular morbidity and mortality [27]. Recently, in patients with stable CAD, Lima et al. [25] reported that the 3 therapeutic regimens (medical therapy, PCI or CABG) had high rates of overall and cardiac-related deaths among diabetic patients compared with non-diabetic cohort.

Compared to non-diabetic patients, we found a roughly doubled prevalence of symptomatic PAD in patients with diabetes enrolled to CR programs (10% *vs.* 5%, $p < 0.0001$). Jude et al. [30] reported that diabetic patients had greater severity of arterial disease in the profunda femoris and all arterial segments below the knee; and diabetic patients were five times more likely to have an amputation (41% *vs.* 11%, OR = 5.4, $p < 0.0001$). Moreover, diabetic patients with PAD had higher mortality rate (51.7% *vs.* 21.6%, OR = 3.1, $p = 0.02$) [30]. Since in patients with CAD the prevalence of previously unrecognized PAD is 15% [31], the present survey suggests the need of a more accurate evaluation of PAD in patients both diabetic and non-diabetic patients entering CR.

This survey also highlighted the higher prevalence of CKD in diabetic patients participating to CR programs compared to the non-diabetic cohort (20% *vs.* 6%, $p < 0.0001$, respectively). This high prevalence of CKD in the diabetic cohort is not surprising, since the interplay role of diabetes and CKD in atherosclerotic disease [32].

Despite the fact that geriatric multidimensional evaluation was performed in about one fourth the patients, the present survey showed that cognitive impairment prevalence (5 *vs.* 2%, $p = 0.0009$) and worsening of cognitive impairment during CR (2.5 *vs.* 1.5%) were significantly higher in diabetic patients compared to the non-diabetic cohort. In fact, diabetes is known to independently affect cognitive status: it has been recently reported that chronically higher blood glucose levels exert a negative effect on cognition, possibly mediated by structural changes in learning-relevant brain areas [33]. Moreover, recent evidence suggests that diabetes may induce epigenetic modifications affecting neuropathological

Table 5 – Drug therapy at hospital discharge after cardiac rehabilitation programs.

	Diabetics ($n = 475$)	Non-diabetics ($n = 1806$)	*p* value
Inhibitors of angiotensin-converting enzyme	273 (57)	984 (54)	0.24
Angiotensin II receptor blockers	98 (20)	289 (16)	0.02
Beta-blockers	330 (69)	1236 (68)	0.66
Nitrates	136 (28)	304 (17)	<0.0001
Diuretics	288 (60)	880 (49)	<0.0001
Statins	363 (76)	1147 (63)	<0.0001
Omega-3 fatty acids	86 (18)	292 (16)	0.31
Oral anticoagulant therapy	92 (19)	512 (28)	<0.0001
Aspirin	339 (71)	1169 (65)	0.006
Digitalis	33 (7)	91 (5)	0.10
Amiodarone	36 (8)	96 (5)	0.06
Calcium channel blockers	108 (23)	328 (18)	0.02
Insulin	160 (34)	51 (3)	<0.0001
Oral hypoglycemic drugs	315 (66)	104 (6)	<0.0001

mechanisms in the brain leading to increased susceptibility to insults associated with neurodegenerative or vascular impairments [34].

The present survey also highlighted that larger proportion of diabetic patients did not perform any type of physical performance test compared to the non-diabetic cohort. This might have prognostic relevance, since the lack of referral to exercise stress testing is by itself a negative prognostic indicator [35].

There were also interesting differences relatively to drugs use. The rather low discharge indication to statin in the total populations is a consequence of the difficulties of adopting in the real clinical world the recommendations of international Guidelines regarding secondary prevention [36].

Finally, complications during CR (particularly re-infarction, worsening of CKD, sternal revision or inotropic support) were higher in diabetic patients compared to the non-diabetic cohort, reflecting the higher clinical risk profile of these patients after an acute cardiovascular event.

4.1. Study limitations

The number of patients with diabetes reported in the present survey is relatively small (about 26% of the overall population), making the study underpowered for an in-depth interpretation. This might be ascribed to the small time-period of the enrolment (two weeks). The combination of data from CR centers offering very different cardiac rehabilitation regimens (*e.g.*, residential *vs*. outpatients) is another confounder. The observational nature of the study cannot rule out that the more severely compromised patients with diabetes were not addressed to CR and, therefore, those described in our study may represent a selected more relatively healthy minority. Moreover, this survey did not collect data regarding modality of exercise training regimen (interval *vs*. continuous) or dose of exercise (in terms of volume and intensity) that can greatly affect the functional and clinical parameters (together with outcome) of patients with diabetes [37–39]. Another major limitation was the lack of information on some important functional and clinical parameters of possible interest and the lack of information regarding the achievement of secondary prevention targets; this was again due to the short-term survey type of study, which collected the essential data in order to optimize the description of the demographic and clinical course of the patients.

Despite these limitations, the survey successfully highlighted crucial differences in the clinical characteristics, risk profile, management and short term outcome in diabetic patients entering CR programs in Italy, compared to non diabetics. Patients with diabetes should not be denied access to CR, provided careful attention to clinical status, possible complications, optimization of drug therapy and close follow-up.

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.diabres.2014.11.006.

REFERENCES

[1] Rauch B, Riemer T, Schwaab B, Schneider S, Diller F, Gohlke H, et al. Short-term comprehensive cardiac rehabilitation after AMI is associated with reduced 1-year mortality: results from the OMEGA study. Eur J Prev Cardiol 2014;21:1060–9.

[2] Giallauria F, Cirillo P, Lucci R, Pacileo M, De Lorenzo A, D'Agostino M, et al. Left ventricular remodeling in patients with moderate systolic dysfunction after myocardial infarction: favorable effects of exercise training and predictive role of N-terminal pro-brain natriuretic peptide. Eur J Cardiovasc Prev Rehabil 2008;15:113–8.

[3] Giallauria F, Galizia G, Lucci R, D'Agostino M, Vitelli A, Maresca L, et al. Favorable effects of exercise-based cardiac rehabilitation after acute myocardial infarction on left atrial remodeling. Int J Cardiol 2009;136:300–6.

[4] Giallauria F, Lucci R, D'Agostino M, Vitelli A, Maresca L, Mancini M, et al. Two year multi-comprehensive secondary prevention program: favourable effects on cardiovascular functional capacity and coronary risk profile after acute myocardial infarction. J Cardiovasc Med (Hagerstown) 2009;10:772–80.

[5] Giannuzzi P, Temporelli PL, Marchioli R, Maggioni AP, Balestroni G, Ceci V, et al. Global secondary prevention strategies to limit event recurrence after myocardial infarction. Arch Intern Med 2008;168:2194–204.

[6] Giallauria F, Acampa W, Ricci F, Vitelli A, Maresca L, Mancini M, et al. Effects of exercise training started within 2 weeks after acute myocardial infarction on myocardial perfusion and left ventricular function: a gated SPECT imaging study. Eur J Prev Cardiol 2012;19:1410–9.

[7] Giallauria F, Acampa W, Ricci F, Vitelli A, Torella G, Lucci R, et al. Exercise training early after acute myocardial infarction reduces stress-induced hypoperfusion and improves left ventricular function. Eur J Nucl Med Mol Imaging 2013;40:315–24.

[8] Tarro Genta F, Eleuteri E, Temporelli PL, Comazzi F, Tidu M, Bouslenko Z, et al. Flow-mediated dilation normalization predicts outcome in chronic heart failure patients. J Card Fail 2013;19:260–7.

[9] Giallauria F, Cirillo P, D'agostino M, Petrillo G, Vitelli A, Pacileo M, et al. Effects of exercise training on high-mobility group box-1 levels after acute myocardial infarction. J Card Fail 2011;17:108–14.

[10] Cirillo P, Giallauria F, Pacileo M, Petrillo G, D'Agostino M, Vigorito C, et al. Increased high mobility group box-1 protein levels are associated with impaired cardiopulmonary and echocardiographic findings after acute myocardial infarction. J Card Fail 2009;15:362–7.

[11] Giallauria F, De Lorenzo A, Pilerci F, Manakos A, Lucci R, Psaroudaki M, et al. Long-term effects of cardiac rehabilitation on end-exercise heart rate recovery after myocardial infarction. Eur J Cardiovasc Prev Rehabil 2006;13:544–50.

[12] Giallauria F, Lucci R, Pietrosante M, De Lorenzo A, Gargiulo G, D'Agostino M, et al. Exercise-based cardiac rehabilitation improves heart rate recovery in elderly patients after acute

myocardial infarction. J Gerontol Ser A Biol Sci Med Sci 2006;61:713–7.
[13] Giallauria F, De Lorenzo A, Pilerci F, Manakos A, Lucci R, Psaroudaki M, et al. Reduction of NT-pro-BNP levels with exercise-based cardiac rehabilitation in patients with left ventricular dysfunction after myocardial infarction. Eur J Cardiovasc Prev Rehabil 2006;13:625–32.
[14] Giallauria F, Lucci R, De Lorenzo A, D'Agostino M, Del Forno D, Vigorito C, et al. Favourable effects of exercise training on N-terminal pro-brain natriuretic peptide plasma levels in elderly patients after acute myocardial infarction. Age Ageing 2006;35:601–7.
[15] Smart N, Meyer T, Butterfield J, Faddy S, Passino C, Malfatto G, et al. Individual patient meta-analysis of exercise training effects on systemic brain natriuretic peptide expression in heart failure. Eur J Prev Cardiol 2012;19: 428–35.
[16] Rinaldi B, Corbi G, Boccuti S, Filippelli W, Rengo G, Leosco D, et al. Exercise training affects age-induced changes in SOD and heat shock protein expression in rat heart. Exp Gerontol 2006;41:764–70.
[17] Soja AM, Zwisler AD, Frederiksen M, Melchior T, Hommel E, Torp-Pedersen C, et al. Use of intensified comprehensive cardiac rehabilitation to improve risk factor control in patients with type 2 diabetes mellitus or impaired glucose tolerance – the randomized DANish StUdy of impaired glucose metabolism in the settings of cardiac rehabilitation (DANSUK) study. Am Heart J 2007;153:621–8.
[18] Mourot L, Boussuges A, Maunier S, Chopra S, Rivière F, Debussche X, et al. Cardiovascular rehabilitation in patients with diabetes. J Cardiopulm Rehabil 2010;30:157–64.
[19] Giallauria F, Vigorito C, Tramarin R, Fattirolli F, Ambrosetti M, De Feo S, et al. Cardiac rehabilitation in very old patients: data from the Italian Survey on Cardiac Rehabilitation-2008 (ISYDE-2008) – official report of the Italian Association for Cardiovascular Prevention. Rehabilitation and Epidemiology (GICR-IACPR). J Gerontol Ser A Biol Sci Med Sci 2010;65A:1353–61.
[20] Giallauria F, Fattirolli F, Tramarin R, Ambrosetti M, Griffo R, Riccio C, et al. Cardiac Rehabilitation in chronic heart failure: data from the Italian SurveY on carDiac rEhabilitation (ISYDE 2008). J Cardiovasc Med (Hagerstown) 2014;15:155–63.
[21] Giallauria F, Fattirolli F, Tramarin R, Ambrosetti M, Griffo R, Riccio C, et al. Clinical Characteristics and Course of Patients Entering Cardiac Rehabilitation with Chronic Kidney Disease: Data from the Italian Survey on Cardiac Rehabilitation. ISRN Rehabilitation, Article ID 807546; 2013. http://dx.doi.org/10.1155/2013/807546, 10 pages.
[22] Folstein MF, Folstein SE, McHugh PR. ''Mini-mental state'': a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98.
[23] Sanidas EA, Brener SJ, Maehara A, Généreux P, Witzenbichler B, El-Omar M, et al. Outcomes in diabetic patients undergoing primary percutaneous coronary intervention for acute anterior myocardial infarction: results from the INFUSE-AMI study. Catheter Cardiovasc Interv 2014;83:704–10.
[24] Brener SJ, Mehran R, Dressler O, Cristea E, Stone GW. Diabetes mellitus, myocardial reperfusion, and outcome in patients with acute ST-elevation myocardial infarction treated with primary angioplasty (from HORIZONS AMI). Am J Cardiol 2012;109:1111–6.
[25] Lima EG, Hueb W, Garcia RM, Pereira AC, Soares PR, Favarato D, et al. Impact of diabetes on 10-year outcomes of patients with multivessel coronary artery disease in the Medicine, Angioplasty, or Surgery Study II (MASS II) trial. Am Heart J 2013;166:250–7.
[26] Kapur A, Bartolini D, Finlay MC, Qureshi AC, Flather M, Strange JW, et al. The Bypass Angioplasty Revascularization in Type 1 and Type 2 Diabetes Study: 5-year follow-up of revascularization with percutaneous coronary intervention versus coronary artery bypass grafting in diabetic patients with multivessel disease. J Cardiovasc Med (Hagerstown) 2010;11:26–33.
[27] Harjai KJ, Stone GW, Boura J, Mattos L, Chandra H, Cox D, et al. Comparison of outcomes of diabetic and nondiabetic patients undergoing primary angioplasty for acute myocardial infarction. Am J Cardiol 2003;91:1041–5.
[28] Bolognese L, Carrabba N, Santoro GM, Valenti R, Buonamici P, Antoniucci D. Angiographic findings, time course of regional and global left ventricular function, and clinical outcome in diabetic patients with acute myocardial infarction treated with primary percutaneous transluminal coronary angioplasty. Am J Cardiol 2003;91:544–9.
[29] Yu CM, Lau CP, Cheung BM, Fong YM, Ho YY, Lam KB, et al. Clinical predictors of morbidity and mortality in patients with myocardial infarction or revascularization who underwent cardiac rehabilitation, and importance of diabetes mellitus and exercise capacity. Am J Cardiol 2000;85:344–9.
[30] Jude EB, Oyibo SO, Chalmers N, Boulton AJ. Peripheral arterial disease in diabetic and nondiabetic patients: a comparison of severity and outcome. Diabetes Care 2001;24:1433–7.
[31] Moussa ID, Jaff MR, Mehran R, Gray W, Dangas G, Lazic Z, et al. Prevalence and prediction of previously unrecognized peripheral arterial disease in patients with coronary artery disease: the Peripheral Arterial Disease in Interventional Patients Study. Catheter Cardiovasc Interv 2009;73:719–24.
[32] Fioretto P, Caramori ML, Mauer M. The kidney in diabetes: dynamic pathways of injury and repair. The Camillo Golgi Lecture 2007. Diabetologia 2008;51:1347–55.
[33] Kerti L, Witte AV, Winkler A, Grittner U, Rujescu D, Flöel A. Higher glucose levels associated with lower memory and reduced hippocampal microstructure. Neurology 2013;81:1746–52.
[34] Wang J, Gong B, Zhao W, Tang C, Varghese M, Nguyen T, et al. Epigenetic mechanisms linking diabetes and synaptic impairments. Diabetes 2014;63:645–54.
[35] Stone PH, Turi ZG, Muller JE, Parker C, Hartwell T, Rutherford JD, et al. Prognostic significance of the treadmill exercise test performance 6 months after myocardial infarction. J Am Coll Cardiol 1986;8:1007–17.
[36] Piepoli MF, Corrà U, Benzer W, Bjarnason-Wehrens B, Dendale P, Gaita D, et al. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. Eur J Cardiovasc Prev Rehabil 2010;17:1–17.
[37] Smart NA, Dieberg G, Giallauria F. Intermittent versus continuous exercise training in chronic heart failure: a meta-analysis. Int J Cardiol 2013;166:352–8.
[38] Smart NA, Dieberg G, Giallauria F. Functional electrical stimulation for chronic heart failure: a meta-analysis. Int J Cardiol 2013;167:80–6.
[39] Smart NA, Giallauria F, Dieberg G. Efficacy of inspiratory muscle training in chronic heart failure patients: a systematic review and meta-analysis. Int J Cardiol 2013;167:1502–7.