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http://www.jrdiabet.ro
Rom J Diabetes Nutr Metab Dis. **20**(3):279-286
doi: 10.2478/rjdnmd-2013-0026

CARDIO-METABOLIC RISK FACTORS CONTROL IN NEWLY DIAGNOSED TYPE 2 DIABETIC SUBJECTS

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received: April 24, 2013 *accepted*: August 19, 2013
available online: September 15, 2013

Abstract

Background and Aims. *The aim of this study was to assess the control of the cardio-metabolic risk factors in subjects with newly diagnosed type 2 diabetes (T2DM) one year after initiating the clinical management.* ***Material and Methods****. We conducted a prospective observational study including 673 persons with newly diagnosed T2DM, registered at the Clinical Center of Diabetes Cluj-Napoca, between 2006-2008.* ***Results:*** *Of the total T2DM subjects who were followed-up until the end of the first year after diagnosis, the proportion of those reaching the optimal goals for major risk factors was 72.1% for HbA1c, 58.6% for blood pressure (BP) and 40.3% for LDL cholesterol. All three goals were met by only 6.9%. Achieving glycemic targets is associated with a lower HbA1c value at diagnosis (OR:0.66, 95%IC: 0.54-0.81). The parameters which were initially identified as associated with achieving the objectives of the clinical management were represented by age, male gender, clinical parameters (HbA1c, body mass index, BP), hypertension, pharmacotherapy.* ***Conclusions:*** *Implementing clinical management in newly diagnosed T2DM subjects resulted in improved glycemic control and cardiovascular risk factors one year after diagnosis. The management of newly diagnosed people with T2DM focused specifically on achieving the glycemic target.*

key words: *Newly diagnosed T2DM, cardio-metabolic risk factors, hemoglobin A1c, blood pressure, LDL cholesterol.*

Background and aims

The prevalence of type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) continue to increase at epidemic proportions [1]. Meanwhile, CVD is the leading cause of morbidity and mortality in people with diabetes. The UKPDS study reported that intensive blood glucose control resulted in a decrease in microvascular complications, while macrovascular complications were not significantly reduced and showed that the prevention of CVD through blood glucose control alone was insufficient [2-4]. As well, a more recent meta-analysis of the effect of intensive glucose control on CV outcomes including data from the UKPDS, ACCORD, ADVANCE and VADT trials showed a

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significant reduction in coronary heart disease (CHD) and CVD events, but no reduction in cardiovascular mortality or total mortality [5]. Aggressive control of hypertension and lowering low-density lipoprotein (LDL) cholesterol levels reduce the risk of cardiovascular events [6]. Therefore, the results from the Steno-2 study support the hypothesis that intensive integrated therapy in high-risk patients with T2DM has the potential to decrease the risk for both microvascular and macrovascular complications and mortality [7,8].

The typical patient with T2DM has multiple cardiovascular risk (CVR) factors, each of which should be treated in accordance with existing guidelines [6]. Initiation of intensive therapy soon after diabetes diagnosis was shown to reduce the risk of microvascular and macrovascular diseases [9].

The aims of our study were: 1) to assess the control of the cardio-metabolic risk factors one year after initiating the clinical management in subjects with newly diagnosed T2DM; 2) to identify the baseline characteristics of the subjects with newly diagnosed T2DM associated with achievement of the goals for glycemia, blood pressure (BP) and LDL- cholesterol one year after diagnosis.

Material and methods

The baseline examination was carried out between 2006-2008 and included 968 individuals with T2DM registered at the Clinical Center of Diabetes Cluj-Napoca. The following inclusion criteria were used for the study: subjects with newly diagnosed T2DM (defined according to World Health Organization criteria [10]), aged ≥ 18 yrs. and availability of subject characteristics at baseline and a year after diagnosis. The final sample size was composed of 673 individuals with T2DM; 295 individuals were excluded (lost of follow-up, unavailability of all clinical data a year after diagnosis).

Diabetes care was based on a complete medical diagnosis and a comprehensive diabetes evaluation, followed by implementation of the clinical management strategy and subsequent evaluation of each patient's medical condition and treatment a year after diagnosis. The following data were evaluated: demographic characteristics (age, gender), medical history (CVD), anthropometric parameters (body mass index (BMI), waist circumference), glycemic control, lipid profile and blood pressure. The treatment of CVR factors was also evaluated. All clinical data were retrieved from the medical records and all patients included in the study were followed for one year. BMI was calculated as weight/height^2. Hypertension was defined as systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 80 mmHg or prescription of antihypertensive therapy [11]. LDL cholesterol was calculated using Friedewald's formula.

The following parameters were used to define the optimal control of cardiovascular risk factors in T2DM subjects : HbA1c <7%, LDL-cholesterol < 100 mg/dL, HDL-cholesterol ≥ 40 mg/dL for men and ≥50 mg/dL for women, triglycerides < 150 mg/dL, BP < 130/80 mmHg and BMI< 25 kg/m^2 [11].

Statistical analysis

We conducted statistical analyses using the SPSS program version 21. Distribution of variables was tested with Kolmogorov-Smirnov test. Data were summarized by means (±SD) for normally-distributed variables, median (1st quartile/ 3rd quartile) for variables with abnormal distribution and percentage for categorical variables. Groups were compared using paired samples t test, chi-square and Wilcoxon-tests as appropriate. Logistic regression was used to ascertain the association between characteristics of newly diagnosed T2DM subjects and achievement of risk factor targets (HbA1c <7.0%, BP <130/80 mmHg and LDL cholesterol

<100 mg/dl) one year after diagnosis. P values < 0.05 were considered to be statistically significant.

Results

A total of 673 patients with newly diagnosed T2DM, 331 (49.2%) men and 342 (50.8%) women, were evaluated at diagnosis of T2DM and a year after. For the entire study group, the mean age at T2DM diagnosis was of 57.7 yrs. The anthropometric and biological characteristics of study subjects at diagnosis and one year after are given in Table 1. The average HbA1c significantly improved from 7.8±1.8% at diagnosis to 6.9±0.9% after one year (p<0.001). SBP and DBP showed significant changes a year after diagnosis (p<0.001) and the mean BP values were 136.1/82.3 mmHg. Although there was an increase in HDL cholesterol (44.2±10.7 mg/dl vs. 43.7±11.0 mg/dl), it was not significantly.

Table 1. Characteristics of T2DM subjects at diagnosis and one year after.

Parameters	At diagnosis	1 yr. after	P value
HbA1c (%)	7.8±1.8	6.9±0.9	<0.001
Plasma glucose (mg/dl)	210.0±90.7	143.7±65.6	<0.001
SBP (mmHg)	144.1±19.4	136.1±15.4	<0.001
DBP (mmHg)	85.8±11.4	82.3±10.7	<0.001
BMI (kg/m^2)	31.5±5.2	31.3±5.3	0.004
Weight (kg)	86.9 ± 16.1	86.2 ± 16.3	<0.001
Waist circumference (cm)	107.1±11.4	106.2±11.6	<0.001
Total-cholesterol (mg/dl)	216.5 (176.7;253.0)	186.0 (158.0;217.0)	<0.001
HDL-cholesterol (mg/dl)	43.7±11.0	44.2±10.7	NS
TG (mg/dl)	168.5 (121.5;252.5)	158.5 (117.0;208.2)	<0.001
LDL-cholesterol (mg/dl)	137.0 (96.4;162.7)	107.4 (85.9;134.2)	<0.001

Data presented are mean (±SD) or median (1st quartile/ 3rd quartile). SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglycerides.

The proportion of those reaching the optimal goals for major risk factors was 72.1% for HbA1c, 58.6% for BP and 40.3% for LDL-cholesterol. As shown in Table 2, all three goals were met by only 6.9% of the study subjects.

Table 2. Proportion of patients reaching the therapeutic goals at diagnosis and one year after.

Management goals	At diagnosis (%)	1 yr. later	p
HbA1c < 7.0%	52.3	72.1	<0.001
BP <130/80 mmHg	26.9	58.6	<0.001
LDL cholesterol < 100 mg/dl	24.6	40.3	<0.001
HDL cholesterol >40mg/dl for men >50mg/dl for women	35.8	40.4	NS
TG < 150mg/dl	35.1	47.0	<0.001
HbA1c+ BP + LDL-cholesterol control	1.5	6.9	NS

Data are presented as number (%).

A significantly higher percentage of men reached the lipid control for the total cholesterol (42.3% vs. 34.3%, p=0.02) and HDL-cholesterol (50.7% vs. 27.6%, p=0.001) a year after diagnosis, as shown in Table 3.

Success rates for glycemic control (HbA1c <7%) appeared to be independent of demographic characteristics (age, sex), clinical parameters (BMI, BP) and CVD prevalence (Table 4). Additionally, as HbA1c levels were lower initially, the HbA1c goal success rate increased a year after (7.1 ± 1.4% vs. 8.3 ± 1.5%, p<0.001).

Table 3. The proportion of patients reaching the therapeutic goals one year after diagnosis according to their gender.

	Men	Women	p
HbA1c < 7.0%	75.0	69.5	NS
SBP <130mmHg	49.6	46.5	NS
DBP <80 mmHg	67.2	60.6	NS
LDL-cholesterol < 100 mg/dl	42.9	37.7	NS
Total cholesterol < 175 mg/dl	42.3	34.3	0.02
HDL-cholesterol >40mg/dl men >50mg/dl women	50.7	27.6	0.001
TG <150 mg/dl	47.2	46.8	NS

Data are presented as number (%). NS, not significant.

Table 4. Characteristics of the study subjects according to their achievement of glycemic control.

Characteristic	HbA1c < 7.0%	HbA1c ≥ 7.0%	P value
Number (%)	72.1	27.9	
Sex: Male (%) Female (%)	75.0 69.5	25.0 30.5	NS
Age (yrs.)	57.1 ± 9.0	56.7 ± 9.9	NS
BMI (kg/m^2)	31.2 ± 5.4	32.6 ± 16.2	NS
SBP (mmHg)	135.7 ± 14.7	135.4 ± 15.9	NS
DBP (mmHg)	81.3 ± 11.0	82.4 ± 10.4	NS
Initial HbA1c (%)	7.1 ± 1.4	8.3 ± 1.5	<0.001
Total-cholesterol (mg/dl)	180.0 (157.0;210.0)	184.5 (162.0;207.2)	0.03
HDL-cholesterol (mg/dl)	45.7 ± 12.3	44.1 ± 9.6	NS
TG (mg/dl)	150.0 (101.5;205.5)	174.5 (122.7;235.2)	<0.001
LDL-cholesterol (mg/dl)	105.8 (84.2;130.0)	109.5 (80.4;128.8)	NS
CVD (%)	19.3	19.5	NS

Data presented are mean (±SD), median (1st quartile/ 3rd quartile) or number (%).

Table 5. Baseline characteristics associated with attainment of cardiovascular risk factor goals one year after diagnosis.

Goals	Baseline caracteristics	OR	95%CI	P
HbA1c < 7.0%	HbA1c	0.66	0.54-0.81	<0.001
LDL-cholesterol < 100 mg/dl	Male gender Total cholesterol Statins	2.09 0.98 2.04	1.19-3.66 0.96-0.99 1.20-3.49	0.01 0.02 0.04
SBP<130mmHg	Age Hypertension BMI SBP DBP	0.97 0.21 0.92 0.93 1.04	0.94-0.99 0.09-0.50 0.88-0.97 0.92-0.95 1.01-1.07	0.03 <0.001 0.001 <0.001 0.001
DBP <80 mmHg	Age SBP DBP	1.02 0.97 0.96	1.003-1.05 0.96-0.99 0.94-0.99	0.02 0.004 0.01

Baseline characteristics of the newly diagnosed T2DM subjects that independently influence achievement of treatment targets for HbA1c, BP and LDL-cholesterol one year after diagnosis, are given in Table 5. Achieving the glycemic control is associated with a lower HbA1c value at diagnosis (OR: 0.66, 95%IC:0.54-0.81).

During the first year after diagnosis, the therapeutic structure changed significantly as shown in Table 6.

We also assessed both at baseline and one year after diagnosis, the pharmacotherapy of BP control in people with hypertension, the pharmacotherapy of lipid control in people with dyslipidemia and also the use of aspirin (Table 7).

Table 6. Evaluation of antihyperglycemic therapy in T2DM one year after diagnosis.

Antihyperglycemic therapy	Initial	1 yr. later	P
Lifestyle alone%	34.0	10.4	<0.001
Oral agents %	55.8	75.8	<0.001
Oral monotherapy %	46.8	44.3	<0.001
Oral drug combination %	9.0	31.1	<0.001
Insulin therapy %	8.8	4.4	<0.001
Insulin + Oral agents %	4.7	9.4	<0.001

Data are presented as number (%).

Table 7. Blood pressure/ lipid management and aspirin therapy.

CVR factors management	Initial	1 yr. after	P
Statin %	39.3	44.0	0.007
Fibrate %	22.4	24.6	NS
ACE inhibitors %	59.6	44.1	<0.001
ARBs %	4.2	4.6	NS
Thiazide diuretics %	39.9	31.4	<0.001
Loop diuretics %	1.6	1.1	NS
B-blockers %	39.1	29.5	<0.001
Calcium channels blockers %	19.8	15.7	0.001
Aspirin %	28.8	36.4	0.001
Aspirin for primary prevention %	24.4	34.2	<0.001
Aspirin for secondary prevention %	44.6	44.1	NS

ACE - angiotensin-converting enzyme; ARBs - angiotensin receptor blockers;

Discussions

The practical implementation of the standards of care for diabetes is not an easy task. The NHANES study (National Health and Examination Survey 2001-2002) showed that among the people with T2DM 50.2% did not achieve the target for HbA1c, 64.66% did not reach the target for LDL-cholesterol, and 53.0% did not achieve the target for BP [12]. Only a multifactorial approach to the clinical management of diabetes, aiming not only at the glycemic control but also at the control of hypertension and dyslipidemia, may reduce the risk of CVD morbidity and mortality as shown by the Steno-2 study [7,8].

During the first year of carrying out the clinical management following the detection of T2DM in our study, a significant reduction in CVR factors was achieved and a good metabolic control was reached. In the Look AHEAD study, all three major goals (HbA1c, BP and LDL-cholesterol) were met by only 10.1% overweight and obese individuals with T2DM, as compared with 6.9% in our study [13]. On the other hand, the glycemic, lipid and BP control were much improved in our study compared to the EPIDIAB data [14].

The most significant results were recorded for the glycemic control. Treatment of T2DM has traditionally focused on glycemic control to decrease the risk of microvascular complications [3].

The parameters which were initially identified as associated with achieving the major objectives of the clinical management one year after the detection were represented by: age, male gender, clinical parameters (HbA1c, the BMI, SBP, DBP), comorbidity (hypertension), pharmacotherapy (statins). These results show

that many of the baseline characteristics of the people newly diagnosed with T2DM may influence the control of cardio-metabolic risk factors. Age, sex, degree of obesity and pharmacotherapy have been also associated in other studies also with the level of the risk factors control in diabetes [13].

Targeting hyperglycemia alone does not reduce the excess risk in diabetes, highlighting the need for aggressive treatment of others risk factors [15]. Despite this, data from multiple sources suggest that those with diabetes do not experience optimal risk factor control compared to those without diabetes [16,17]. In this study it was ascertained that the other cardiovascular risk factors (dyslipidemia, hypertension) benefited from less attention compared to glycemia, as suggested by the much lower percentage in reaching the established objectives. International treatment guidelines consider DM a high-risk condition for developing of CVD and treatment with cardioprotective agents such as statins, ACE inhibitors and aspirin are highly recommended for many diabetic patients [6,18].

The AUDIT study revealed a disparity between lipid screening and control in T2DM patients [19]. Although LDL-C is not usually elevated in T2DM relative to matched individuals without T2DM, it is one of the most important modifiable CVD risk factors [20]. LDL cholesterol-targeted statin therapy remains the preferred strategy [18]. However, statin therapy was recommended for a reduced number of people (44% of those with dyslipidemia) and only half of the people with CVD received statin therapy. Studies examining possible benefits of lipid lowering with fibrates in diabetes have given inconsistent results [6]. Nevertheless, 24.6% of the individuals in our study received fibrate treatment one year after the diagnosis, of whom 9.1% in the form of statin-fibrate combined therapy.

Significantly fewer women than men reached the current treatment goals for total cholesterol and HDL cholesterol. Gender differences in CVR factor treatment and control have been reported previously both in diabetic and non-diabetic patients [21,22].

In many studies, the proportion of individuals with diabetes who achieved hypertension control was low (about only one third of individuals with diabetes and hypertension) and also individuals with diabetes were less likely to achieve hypertension control than those without diabetes [23,24]. The results of the present study may be explained in part by the fact that we used a lower threshold (< 130/80 mmHg) for hypertension control among individuals with diabetes, which is harder to achieve. In people with diabetes, inhibitors of the renin-angiotensin system may have unique advantages for initial or early theraphy of hypertension [18]. ACE inhibitors constituted the most recommended therapeutic agent in our study (59.6% at diagnosis and 44.1% a year after the diagnosis), whereas ARBs were recommended for a reduced number of people (4.2-4.6%).

There were no changes in the treatment with aspirin in people with CVD (44.1% vs. 44.6%), but the recommendation of aspirin for primary prevention therapy increased (34.2% vs. 24.4%). The studies have shown that the effects of aspirin therapy in people with diabetes are smaller than those for the general population, which has lead to a conservative approach about aspirin therapy for CVD prevention in people with diabetes [25]. The role of aspirin in primary prevention remains unproven [6]. However, antiplatelet therapy with aspirin is no longer recommended for people with diabetes who do not have clinical evidence of CVD [18].

It is vital in T2DM patients to lower their CVD risk and prevent an epidemic of CVD morbidity and mortality and a parallel increase in healthcare costs [26]. Further efforts are needed to aggressively control CVD risk factors among individuals with newly diagnosed diabetes [16]. Targeting multiple markers of

CVD risk hopefully offers the best chance of improving CVD outcomes [15].

Conclusions

Implementing of the clinical management for the people with newly diagnosed T2DM resulted in improved glycemic control and cardiovascular risk factors. The practical implementation of standards of care for diabetes from the perspective of achieving short-term therapeutic goals proved difficult. The management of newly diagnosed people with T2DM focused specifically on achieving the glycemic target. The results of this study highlight the need for diabetes management to be directed towards the global cardiovascular risk. Our results also show that many of the baseline characteristics of the people newly diagnosed with T2DM may influence the control of cardio-metabolic risk factors one year after diagnosis.

REFERENCES

1. **Schwartz S, Kohl BA**. Type 2 diabetes mellitus and the cardiometabolic syndrome: impact of incretin-based therapies. *Diabetes Metab Syndr Obes* 3 :227–242, 2010.

2. **Stratton IM, Adler AI, Neil HA et al.** Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 321: 405-412, 2000.

3. **UK prospective Diabetes Study (UKPDS) Group**. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type diabetes (UKPDS 33). *Lancet* 352: 837-853, 1998.

4. **UK prospective Diabetes Study (UKPDS) Group**. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 352: 854-865, 1998.

5. **Turnbull FM, Abraira C, Anderson RJ et al.** Intensive glucose control and macrovascular outcomes in type 2 diabetes. *Diabetologia* 52: 2288-2298, 2009.

6. **The European Society of Cardiology**. European guidelines on cardiovascular disease prevention in clinical practice (version 2012). *Eur Heart J* 33: 1635-1701, 2012.

7. **Pedersen O, Gaede P**. Intensified multifactorial intervention and cardiovascular outcome in type 2 diabetes: the Steno-2-study. *Metabolism* 52: 19-23, 2003.

8. **Gaede P, Lund-Andersen H, Parving HA, Pedersen O**. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 358: 580-581, 2008.

9. **Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA**. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 359: 1577–1589, 2008.

10. **World Health Organization**. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia. Geneva: World Health Organization [online]. 2006 [cited 2012 November]; Available at: http: //www.who.int.

11. **American Diabetes Association**. Standard of Medical Care in Diabetes-2012. *Diabetes Care* 35[Suppl 1]: S11-S63, 2012.

12. **Malik S, Lopez V, Chen R et al.** Undertreatment of cardiovascular risk factors among persons with diabetes in the United States. *Diabetes Res Clin Pract* 77: 126-133, 2007.

13. **Bertoni AG, Clark JM, Feeney P et al.** Suboptimal control of glycemia, blood pressure, and LDL cholesterol in overweight adults with diabetes: the Look AHEAD Study. *J Diabetes Complications* 22: 1-9, 2008.

14. **Hâncu N, Niţă C**. Diabetul Zaharat: Provocarea Continuă. In: *Farmacoterapia diabetului zaharat*. Hâncu N, Roman G, Vereşiu IA, eds. 2nd ed. Editura Echinox, Cluj-Napoca, 1-4, 2008.

15. **Erdmann E.** Diabetes and cardiovascular risk markers. *Curr Med Res Opin* 21[Suppl.1]: S21-S28, 2005.

16. **Preis SR, Pencina MJ, Hwang SJ et al.** Trends in cardiovascular disease risk factors in individuals with and without diabetes mellitus in the Framingham Heart Study. *Circulation* 120: 212-220, 2009.

17. **George PB, Tobin KJ, Corpus RA, Devlin WH, O' Neil**. Treatment of cardiac risk factors in diabetic

patients: How well do we follow the guidelines? *Am Heart J* 142: 857-863, 2001.

18. American Diabetes Association. Standards of medical care in diabetes-2013. *Diabetes Care* 36[Suppl.1]: S11-S66, 2013.

19. Leiter LA, Betteridge DJ, Chacra AR et al. AUDIT study. Evidence of global undertreatment of dyslipidaemia in patients with type 2 diabetes mellitus. *Br J Diabetes Vasc Dis* 6: 31–40, 2006.

20. Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta analysis of data from 170 000 participants in 26 randomised trials. *Lancet* 376: 1670-1681, 2010.

21. Eriksson M, Zethelius B, Eeg-Olofsson K, Nilsson PM, Gudbjörnsdottir S, Cederholm J. Blood lipids in 75,048 type 2 diabetic patients: a population-based survey from the Swedish National diabetes register. *Eur J Cardiovasc Prev Rehabil* 18: 97-105, 2011.

22. Winston GJ, Barr RG, Carrasquillo O, Bertoni AG, Shea S. Sex and racial/ethnic differences in cardiovascular disease risk factor treatment and control among individuals with diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care* 32: 1467-1469, 2009.

23. Aparasu RR, Aparasu A. Hypertension management in outpatient visits by diabetic patients. *Res Social Adm Pharm* 4: 284 –291, 2008.

24. Zannad F, Agabiti-Rosei E. Profile of patients with type 2 diabetes in France and Italy. *J Hypertens* 26[Suppl 3]: S3-S6, 2008.

25. International Diabetes Federation 2012. Clinical Guideline Task Force. Global Guidelines for type 2 diabetes [online]. 2012 [cited 2012 November]; Available at: http://www.idf.org/sites/default/files/IDF%20T2DM%20Guideline.pdf

26. Comaschi M, Coscelli C, Cucinotta D et al. Cardiovascular risk factors and metabolic control in type 2 diabetic subjects attending outpatient clinics in Italy: The SFIDA (survey of risk factors in Italian diabetic subjects by AMD) study. *Nutr Metab Cardiovasc Dis* 15: 204-211, 2005.