The Prevalence of Heart Failure in Hospitalized Patients with Type 2 Diabetes Mellitus and Coronary Artery Disease in Albania

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Abstract: _Aim_: _The aim of our study is to asses the prevalence of heart failure in patiens with diabetes mellitus type 2 and coronary artery disease in hospitalized patients in the department of cardiology during a six month period._ _Methods and results_: _Among 228 patients enrolled in this study, the overall prevalence of congestive heart failure in the whole study population was 32%(73/228). The prevalence of congestive heart failure in patients with coronary artery disease was 36.5%(58/159) and in patients with diabetes was 34.3% (60/175)._ _Conclusion_: _The high prevalence of heart failure is patient with both diabetes mellitus and coronary artery disease rises the awearness for a good glicemic control, therapeutic approaches and the menagment of cardiovascular risk factors._

Keywords: T2DM (type 2 diabetes mellitus), CAD (coronary artery disease), HF (Heart Failure), BMI (body mass index kg/m^2), HbA1C (glicosilated hemoglobin A1C), diastolikdis function, ischemic cardiomyopathy, ACS (acute coronary syndrome).

1. Introduction

The increasing prevalence of DM worldwide has led to a situation where approximately 360 million people had DM in 20111, of whom more than 95% would have had DMT2[1]. This number is estimated to increase to 552 million by 2030. CAD hypertension and diabetic cardiomyopathy are long-term complications of DM , resulting in diabetic heart failure[2].Heart failure and T2DM frequently co-exist, each adversely affecting the natural course of the other.The prevalence of risk factors for heart failure is common in patients with diabetes, among which CAD and hypertension are the most important. In addition, dysglicaemia may itself have an unfavorable effect on miocardium. This has led to recognition of a clinical entity labelled as DM cardiomyopathy, in which compromised diastolik function is an early feature[1].

Diabetic and nondiabetic subjects share common causes of HF, such as ischemic heart disease, hypertension, left ventricular hypertrophy, atrial fibrillation, and valvular disease. The incremental HF risk with diabetes is not completely attributable to these common risk factors, however, suggesting increased myocardial vulnerability in the setting of diabetes and probable synergistic effects between such factors and diabetes that increase HF risk, yielding the concept of "diabetic cardiomyopathy"[3, 4].Given the high prevalence in patients with diabetes, ischemic heart disease remains the principal risk factor for HF in patients with diabetes both in the chronic ambulatory setting and after ACS events. In addition to the burden of coronary atherosclerosis, other contributors to this increased risk may include increased prevalence of silent or atypical symptoms of ischemia delaying diagnosis and intervention, suboptimal use of therapeutic interventions, disturbed sympathovagal balance, prothrombotic milieu that may attenuate benefit of antithrombotic therapies, impaired coronary endothelial function, and disordered ischemic myocardial metabolism[5, 6]. In aggregate, these effects and others probably increase ischemic burden, increase infarct size, and adversely affect remodeling in the setting of ischemic heart disease and ACS events. Affecting both ischemic heart disease and HF risk, hypertension prevalence exceeds 70% in populations with diabetes. Among patients with type 2 diabetes, HF risk increases 12% for every increment of 10 mm Hg in systolic blood pressure [7].Currently, the leading cause of heart failure in developed countries is CAD[8].In the United States, CAD and its complications account for two thirds to three fourths of all cases of heart failure. In many patients, the progressive nature of heart failure reflects the progressive nature of the underlying CAD. The term _ischemic cardiomyopathy_ is used for the clinical syndrome in which one or more of the pathophysiologic features just discussed result in LV dysfunction and heart failure symptoms[9]. This condition is the predominant form of heart failure related to CAD. Additional complications of CAD that may become superimposed on ischemic cardiomyopathy and precipitate heart failure are the development of LV aneurysm and mitral regurgitation caused by papillary muscle dysfunction. Considerably less is known about the prevalence of the combination of diabetes, CAD and heart failure in Albania and this is why we conducted this study.

2. Methods

This was a case-series study including228 patients hospitalized at the University Hospital Center in Tirana, Albania during a 6 month-period in 2013. All patients were measured fasting blood glucose, 2-hour post-prandial glucose, HbA1C, lipids in the blood, CK, CK-MB, Troponin I.

In addition, data collection included measurement of weight and height (based on which, the body mass index [BMI] was calculated), and administration of a structured questionnaire inquiring about the age, sex and socioeconomic characteristics of study participants. Furthermore, for all participants it was performed a resting electrocardiography,

exercise electrocardiography, echocardiography and coronarography. Heart failure was defined as an ejection function below 50%. CAD was defined by the presence of significant stenosis in coronary artery and diabetes as FPG ≥126 mg/dl, 2h pos tprandial glucose ≥200mg/dl or HbA1c ≥6.5 %.

Fisher's exact test was used to compare the distribution of socio-demographic characteristics among patients with diabetes and their counterparts without diabetes. Similarly, Fisher's exact test was employed to compare the proportion of coronary artery disease in patients with and without congestive heart failure. In all cases, a p-value≤0.05 was considered as statistically significant.

SPSS (Statistical Package for Social Sciences, version 19.0) was used for data analysis.

3. Results

Of the overall study population (N=228), 74(32.5%) females and 154(67.5%) males, there were 73 (32%) patients with congestive heart failure. There were 175(76.7%) patients with T2DM and 159(69.7 %) patients with CAD.

The overall prevalence of congestive heart failure in the whole study population was 32% (73/228). 2. The prevalence of congestive heart failure in patients with coronary artery disease was 36.5% (58/159) and in patients with diabetes was 34.3% (60/175).

Mean HBA1C value in patients with congestive heart failure was 8.2±1.5, whereas in patients without congestive heart failure it was 8.1±1.7. This small difference was not statistically significant though (Mann Whitney U-test: P=0.24).There was no evidence of a trend linked with age in the prevalence of congestive heart failure in diabetic patients neither in men nor in women (P=0.67). There was no evidence of a significant association between congestive heart failure and BMI. Hence, mean BMI in patients with congestive heart failure was 27.4±3.2, whereas in patients without congestive heart failure it was 27.2±2.9 (Mann Whitney U-test: P=0.52).Among 107 patients who were treated with insulin the prevalence of congestive heart failure was 43% (N=46), whereas among 119 patients who did not receive insulin the prevalence of congestive heart failure was 22.7% (N=27). This difference between the two groups was highly statistically significant (P=0.002).

Table 1 presents the prevalence of diabetes by selected demographic characteristics in patients with congestive heart failure.

Of 73 patients with congestive heart failure, 60 (82.2%) of them had diabetes mellitus, whereas 13 (17.8%) further subjects did not have diabetes mellitus.

There was no statistically significant sex-difference in the prevalence of diabetes, notwithstanding a higher proportion in women than in men (90.9% vs. 78.4%, respectively, P=0.32).

The prevalence of diabetes was the highest (100%) among patients aged 80 years or older.

Furthermore, the prevalence of diabetes was the highest among Roma community compared with the ethnic Albanians regardless of the lack of statistical significance (100% vs. 80%, respectively, P=0.34).

Table 1: Prevalence of diabetes by selected demographic characteristics in Albanian patients with congestive heart failure (N=73)

Variable	With diabetes (N=60)	No diabetes (N=13)	P-value[†]
Sex: Women Men	20 (90.9%)[*] 40 (78.4%)	2 (9.1%) 11 (21.6%)	0.320
Age-group: 40-59 years 60-79 years ≥80 years	18 (81.8%) 39 (81.3%) 3 (100%)	4 (18.2%) 9 (18.8%) 0 (-)	0.711
Ethnic group: Ethnic Albanian Roma minority	53 (80.3%) 7 (100%)	13 (19.7%) 0 (-)	0.339

[*] Absolute numbers and row percentages (in parentheses).
[†] P-values from Fisher's exact test.

Another analysis was conducted in the overall sample of patients (N=228) in order to assess the relationship between congestive heart failure and coronary artery disease. There were 51 cases with missing data for at least one of these two key variables. Hence, this analysis included 177 patients with complete data on congestive heart disease status and presence of coronary artery disease.

In this sample of 177 patients, the prevalence of coronary artery disease was 98.3% in the subjects with congestive heart failure which was significantly higher compared with 85.6% in those without congestive heart failure (P=0.007) [Table 2].

Table 2: Prevalence of congestive heart failure in Albanian patients with and without coronary artery disease (N=177)

CHF	Parameter	CAD		Total
		No	Yes	
No	Number	17	101	118
	%	94.4%	63.5%	66.7%
Yes	Number	1	58	59
	%	5.6%	36.5%	33.3%
Total	Number	18	159	177
	%	100.0%	100.0%	100.0%
P-value from Fisher's exact test: P=0.007				

The prevalence of congestive heart failure in patients with diabetes was 34.3% (60/175), whereas among patients without diabetes it was 25.5%, as shown in the table below. This difference between two groups was not statistically significant (P=0.307).(Table 3).

Table 3: Prevalence of congestive heart failure in Albanian patients with and without diabetes, (N=226)

CHF	Parameter	Diabetes		Total
		Yes	No	
No	Number	115	38	153
	%	65.7%	74.5%	67.7%
Yes	Number	60	13	73
	%	34.3%	25.5%	32.3%
Total	Number	175	51	226
	%	100.0%	100.0%	100.0%
P-value from Fisher's exact test: P=0.307				

Another analysis was conducted in the sample of the patients with diabetes (N=173) in order to assess the prevalence of diastolic dysfunction. In this subsample, the prevalence of diastolic dysfunction was 45.1% (78/173).

The prevalence of diastolic dysfunction was higher in male patients (59.5%) compared with their female counterparts (46.8%), but this difference was not statistically significant (P=0.114) [Table 4].

Table 4: Prevalence of diastolic dysfunction in patients with diabetes by sex (N=173)

Diastolic dysfunction	Parameter	Sex		Total
		Females	Males	
Yes	Number	33	45	78
	%	53.2%	40.5%	45.1%
No	Number	29	66	95
	%	46.8%	59.5%	54.9%
Total	Number	62	111	173
	%	100.0%	100.0%	100.0%
P-value from Fisher's exact test: P=0.114				

The prevalence of diastolic dysfunction was the highest (50%) among patients with diabetes aged 80 years or older, notwithstanding the lack of statistical significance compared with the other age-groups (P=0.62).

In addition, the prevalence of diastolic dysfunction was higher among Roma patients compared with the ethnic Albanians, but this finding was not statistically significant too (50% vs. 44%, respectively, P=0.64).

4. Discussion

The prevalence of heart failure in a general population is 1 – 4 % and 0.3 – 0.5 % of the patients have both heart failure and T2DM. Studies in heart failure populations reveal a prevalence of T2DM from 12 – 30%, rising with age[10, 11]. The prevalence of DM in a general population is 6 – 8% but, as reviewed by McDonald et al., it is higher in people with sympomatic heart failure (12 – 30%) increasing towards 40% among hospitalized patients.[12]

In the sample of our study we found an association between T2DM and heart failure. We found that DM is a risk factor for heart failure and the incidence of heart failure increases rapidly in patients with both T2DM and CAD. Also we found that the incidence of heart failure rising with age, and even there is a trend of sex difference between men and women in the middle age dominantly in men, with the progression of age this trend tend to be equal. In Roma patients the prevalence of heart failure and diabetes is higher than in the ethnic Albanian patients.

Diasatolicdisfunction in our sample was higher in diabetic patients compared with non- diabetic patients, and its prevalence was higher in Roma patients compared with ethnic Albanians.

DM and heart failure did not predict each other independently, although fasting glucose and BMI were significant risk factors, both for glucose disturbances and heart failure, in the Reykjavik study[11].The overall prevalence of congestive heart failure in the whole study population we examined was 32% (73/228). The prevalence of congestive heart failure in patients with diabetes was 34.3% (60/175) . The prevalence of congestive heart failure in patients with coronary artery disease was 36.5% (58/159). Several clinical correlates are independent risk factors for the development of heart failure in T2DM, including high HbA1C, increased body mass index(BMI), advancing age, associated CAD, retinopathy and insulin use. Also, in recent studies, end- stage renal disease, nephropathy, proteinuria and albuminuria, retinopathy and duration of T2DM were associated with heart failure and its progression [13].Data from our study we conducted find that Among 107 patients who were treated with insulin the prevalence of congestive heart failure was 43% (N=46), whereas among 119 patients who did not receive insulin the prevalence of congestive heart failure was 22.7% (N=27). This difference between the two groups was highly statistically significant (P=0.002). There was no evidence of a significant association between congestive heart failure and BMI. Hence, mean BMI in patients with congestive heart failure was 27.4 ± 3.2, whereas in patients without congestive heart failure it was 27.2 ± 2.9 (Mann Whitney U-test: P=0.52). This may be attributed to the small sample of the study. Mean HBA1C value in patients with congestive heart failure was 8.2 ± 1.5, whereas in patients without congestive heart failure it was 8.1 ± 1.7. This small difference was not statistically significant though (Mann Whitney U-test: P=0.24). In the Framingham study, the relative risk of heart failure in patients with T2DM (age 45 – 74 years) was doubled for men and six times as high in women.[14] The high incidence of heart failure in patients with T2DM was also confirmed in the National Health and Nutrition examination survey, which revealed T2DM as an independent risk factor for heart failure in T2DM, compared with non – T2DM.[7] The prevalence increased rapidly with age, and heart failure with preserved LVEF was common in women than men[15].In our study there was no statistically significant sex-difference in the prevalence of diabetes, notwithstanding a higher proportion in women than in men (90.9% vs. 78.4%, respectively, P=0.32). There was no evidence of a trend linked with age in the prevalence of congestive heart failure in diabetic patients neither in men nor in women (P=0.67).The prevalence of heart failure varies somewhat in different studies. The prevalence of heart failure has been estimated to be 0.6 – 6.2 % in Swedish men and this increases with age. This is similar to the overall prevalence of heart failure among genders in the Rotterdam population and the Reykjavik Study[16-18].

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5. Conclusions

In summary, HF is common among patients with diabetes and coronary artery disease, and in addition to usual pathologic contributors to HF in common with the overall population, numerous metabolic and pathologic abnormalities associated with diabetes may explain the increased HF risk and inform drug development efforts toward new therapeutic targets especially for some specific group of patients such as the elderly, those with insulin therapy , obesity patients etc.. Therefore, in addition to ongoing research in this area, clinical efforts should focus on the optimal application of existing risk-mitigating therapies in patients with HF diabetes and CAD.

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