

*Correspondence: Roxana CHIRIȚĂ
Clinical Psychiatric Hospital "Socola",
Șos. Bucium no. 34, 700282, Iași, Romania
E-mail: d.stigma@gmail.com*

Date of Submission: December, 12, 2011 / Acceptance: March, 06, 2012

SOMATIC COMORBIDITIES IN PATIENTS WITH BIPOLAR DISORDER (B)

Maria Magdalena DUMITRU, Vasile CHIRIȚĂ, Roxana CHIRIȚĂ

Maria Magdalena DUMITRU: M. D., Resident in psychiatry, Clinical Psychiatric Hospital "Socola", Iași, Romania

Vasile CHIRIȚĂ: M. D., Ph. D., Professor, Dept. of Psychiatry, University of Medicine and Pharmacy "Gr. T. Popa" Iași; Senior Psychiatrist, Clinical Psychiatric Hospital "Socola", Iași, Romania; Member of Romanian Academy of Medical Sciences

Roxana CHIRIȚĂ: M. D., Ph. D., Professor, Dept. of Psychiatry, University of Medicine and Pharmacy "Gr. T. Popa" Iași; Senior Psychiatrist, Clinical Psychiatric Hospital "SOCOLA", Iași, Romania

ABSTRACT:

Bipolar patients have a high risk for somatic comorbidities that need to be treated by non-psychiatrist medics. Factors related to unhealthy lifestyle, disease and treatment may confer some additional risk of morbidity in people with bipolar disorder.

Objective: The primary endpoint of the study was to detect risk factors for the development of somatic comorbidities in patients with bipolar disorder which will allow an appropriate treatment, in order to improve their quality of life.

Methods: The study was conducted by interviewing and physical examination of a group of 57 consecutive patients who were hospitalized between 1st of February to 30th of March 2011, in the Clinical Hospital of Psychiatry "Socola" Iași and were diagnosed with bipolar disorder according to DSM-IV-TR criteria.

Results: Patients age range was 28 to 71 years (SD 8.24 years). Of the subjects, 59,54 % were female and 40,35 % men. The study shows that 66.6 % of patients with bipolar disorder smoked regularly, and 40.4 % consumed alcohol abusively. The most common somatic diseases associated were hypertension, dyslipidemia, alcoholism, arthrosis, obesity, liver disease, neuropathy, angina pectoris and type 2 diabetes mellitus. Metabolic syndrome criteria were met by half of patients.

Conclusions: Most somatic diseases recorded were associated metabolic syndrome and other disorders, usually caused by an unhealthy diet and lifestyle. The prevalence of the metabolic syndrome in patients with bipolar disorder is alarmingly high. Interventions specifically designed for preventing and treating the metabolic syndrome and its components in patients with bipolar disorder are needed.

Keywords: *bipolar disorder, somatic comorbidities, metabolic syndrome*

REZUMAT:

Pacienții cu tulburare bipolară prezintă un risc crescut pentru comorbidități somatice care trebuie să fie tratate de medici de alte specializări medicale. Factorii legați de stilul de viață nesănătos, boală și tratament ar putea conferi un risc suplimentar de morbiditate la acești pacienți.

Obiectiv: Obiectivul primar al studiului a fost detectarea factorilor de risc pentru dezvoltarea comorbidităților somatice la pacienții cu tulburare bipolară, ceea ce va permite un tratament adecvat pentru îmbunătățirea calității vieții lor.

Metoda: Studiul a fost realizat prin interviuarea și examinarea fizică a unui grup de 57 de pacienți consecutivi care au fost internați în perioada 1 februarie – 30 martie 2011, în Spitalul Clinic de Psihiatrie "Socola" Iași și au fost diagnosticați cu tulburare bipolară în conformitate cu criteriile DSM-IV-TR.

Rezultate: Vârsta pacienților a fost cuprinsă în intervalul de vârstă de la 28 la 71 ani (DS 8.24 ani). Dintre pacienți, 59,54 % au fost femei și 40,35 % bărbați. Studiul arată că 66 % dintre pacienții cu tulburare bipolară fumează cu regularitate, iar 40 % consumă alcool în mod abuziv. Cele mai comune boli somatice asociate au fost hipertensiunea arterială, dislipidemia, alcoolismul, artroza, obezitatea, bolile hepatice, neuropatia, angina pectorală și diabetul zaharat de tip 2. Criteriile sindromului metabolic au fost îndeplinite de aproximativ jumătate dintre pacienți.

Concluzii: Pacienții cu tulburare bipolară prezintă o proporție ridicată de abuz de alcool și fumat. Cele mai multe boli somatice înregistrate au fost asociate sindromului metabolic și altor tulburări cauzate de obicei de dieta nesănătoasă și de stilul de viață. Prevalența sindromului metabolic la pacienții cu tulburare bipolară este alarmant de mare. Avem nevoie de intervenții concepute special pentru prevenirea și tratarea sindromului metabolic și a componentelor sale la pacienții cu tulburare bipolară.

Cuvinte-cheie: *tulburare bipolară, comorbidități somatice, sindrom metabolic*

INTRODUCTION

Bipolar disorder is a severe lifelong psychiatric illness that is at high risk of recurrence and increased morbidity over time. For the full spectrum of bipolar disorder prevalence is estimated between 4 to 12 %. (1, 2)

Recovery from acute episodes may last up to six months, and symptomatic remission may occur after 8 months or more if repeated relapses. (3)

Current guidelines recommend mood stabilisers in combination with atypical antipsychotics as the first-line treatment approach for severe mania or mixed episodes and in the long-term maintenance setting for patients who fail to respond to monotherapy treatments and continue to experience sub-threshold symptoms or relapse. (4)

Factors related to lifestyle, disease and treatment in people with bipolar disorder may confer an additional risk of morbidity and mortality by increasing prevalence of obesity, metabolic syndrome, diabetes mellitus and cardiovascular complications. Compared with the general population, mortality caused by cardiovascular problems and embolism, and morbidity due to obesity and type 2 diabetes is increased in patients with bipolar disorder. (5)

Medication may be a contributing factor, because antipsychotics can induce or exacerbate metabolic disorders. Some of these drugs slightly affects metabolism, while others can contribute to more serious damage metabolism. Young people or people without previous exposure to antipsychotics may be more prone to this side effect. (6)

OBJECTIVES

Most studies cited in the literature are limited to the clinical aspect of the antipsychotic treatment and not on somatic comorbidities independent of it. This study sought to evaluate the presence of real medical panorama of the bipolar patient and to detect risk factors for the development of

somatic comorbidities in patients with bipolar disorder which will allow an appropriate treatment, in order to improve the quality of their life.

MATERIAL AND METHODS

A cross-sectional study was performed by interviewing and physical examination of a group of 57 consecutive patients who were hospitalized between 1st of February and 30th of March 2011, in Clinical Hospital of Psychiatry “Socola” Iași and were diagnosed with bipolar disorder, according to the DSM-4 TR criteria.

Inclusion criteria were obtaining informed consent, an age over 18 years, present diagnosis of bipolar affective disorder according to DSM-IV-TR criteria.

The study includes a descriptive analysis of demographic characteristics, medical history, disease characteristics and clinical management. Statistical analysis of the data was obtained by making use of the ANOVA statistical and mathematical analysis.

RESULTS AND DISCUSSIONS

The study was conducted by interviewing and physical examination of a group of 57 patients, who required specialized care for bipolar disorder, in the Psychiatric University Hospital “Socola” Iași. Patients’ age range was between 28 to 71 years (SD 8.24 years). A descriptive image of demographic data for patients enrolled in the study is present in Table I.

Tab. I: *Demographic characteristics of patients*

Demographic characteristics of patients	Value
Sex, %	
Female	59,54
Male	40,35
Average age, years	52.5
Place of origin, %	
Urban	56.15
Rural	43.85
Cohabitation, %	
Married	33.4
Divorced	24.5
Cohabiting	22.8
Single	14.0
Widower	5.3
Average of education, years	10.57
Employment status, %	
Employee	8.8
Retired	61.4
Unemployed	24.6
Disabled	5.3
Unhealthy habits, %	
Smoking	66.7
Alcohol abuse	40.4

The most common somatic diseases associated were hypertension, dyslipidemia, alcoholism, arthrosis, obesity, liver disease, neuropathy, angina pectoris and type 2 diabetes mellitus. (Fig. 1)

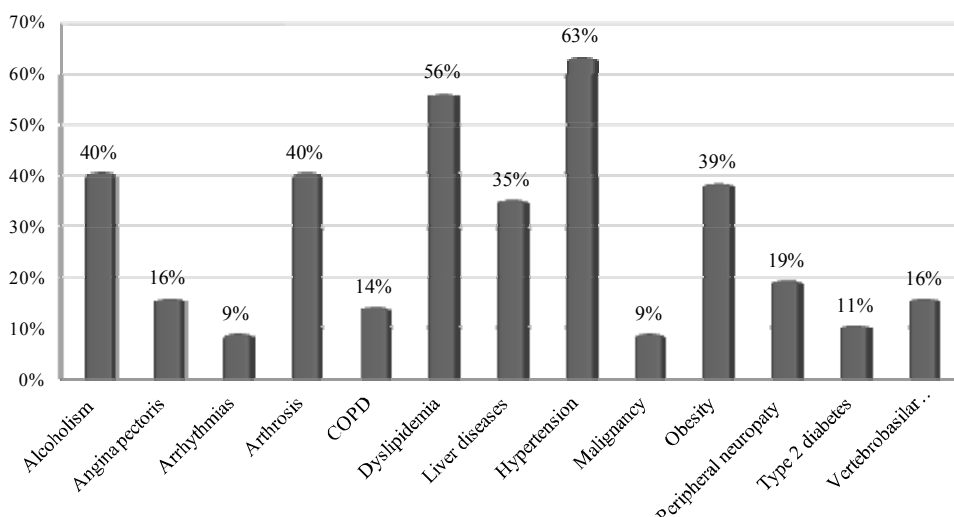


Fig. 1: *Percentage distribution of related diseases*

According to European Society of Hypertension criteria (Tab. II), subjects with systolic blood pressure > 140 mm Hg and/or diastolic blood pressure > 90 mm Hg, as well as those with previous history of hypertension and taking current antihypertensive medication for control blood pressure, were considered hypertensives. (7)

Tab. II: *Definitions and classification of blood pressure levels (mmHg) according to European Society of Hypertension criteria*

Category	Systolic	Diastolic
Optimal	< 120	and < 80
Normal	120 – 129	and/or 80 – 84
Normal high	130 – 139	and/or 85 – 89
Grade 1 hypertension	140 – 159	and/or 90 – 99
Grade 2 hypertension	160 – 179	and/or 100 – 109
Grade 3 hypertension	≥ 180	and/or ≥ 110
Isolated systolic hypertension	≥ 140	and < 90

Hypertension was present in 63 % of patients, a 1.7 higher rate compared to that found in the general population. The percentage of subjects with optimal, normal or high blood pressure is shown in Fig. 2 of the global sample. (8)

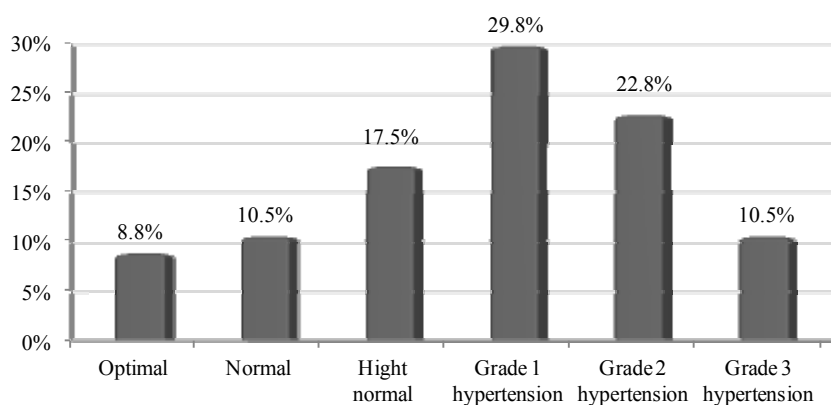


Fig. 2: *The percentage of bipolar patients with optimal, normal or high blood pressure*

Among patients who had blood pressure values higher than 140/90 mmHg, 33.3 % were not previously diagnosed with hypertension. Of patients with known hypertension, 22.7 % were receiving monotherapy with angiotensin-converting-enzyme inhibitor and the rest received bitherapy with angiotensin-converting-enzyme inhibitor and diuretic for 30 % of patients, or beta blockers and diuretic for 10 % of patients. (Fig. 3)

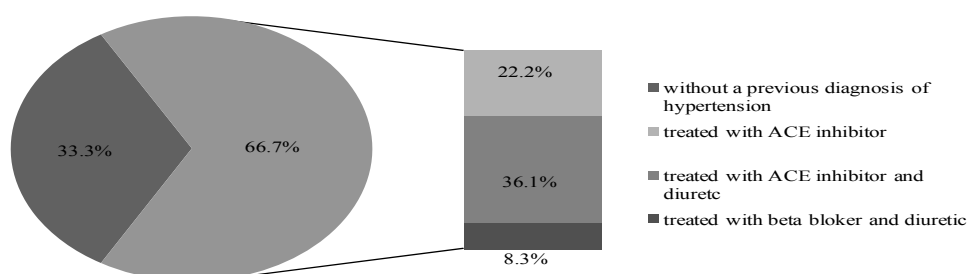


Fig. 3: *Distribution of patients with hypertension according to followed treatment*

Subjects on lipid lowering medication or those diagnosed with total cholesterol > 200 mg/dl were considered hyper-cholesterolemics. In this study, mixt dyslipidemia was present at 64.9 % of bipolar patients, 47.4 % had hypercholesterolemia or were on a cholesterol-lowering medication, 42.1 % had hypertriglyceridemia, and 33.3 % had low values of high-density lipoprotein cholesterol. (Fig. 4) The percent of patients with hyper-cholesterolemia was 1.97 times higher than the one found in general population. (8)

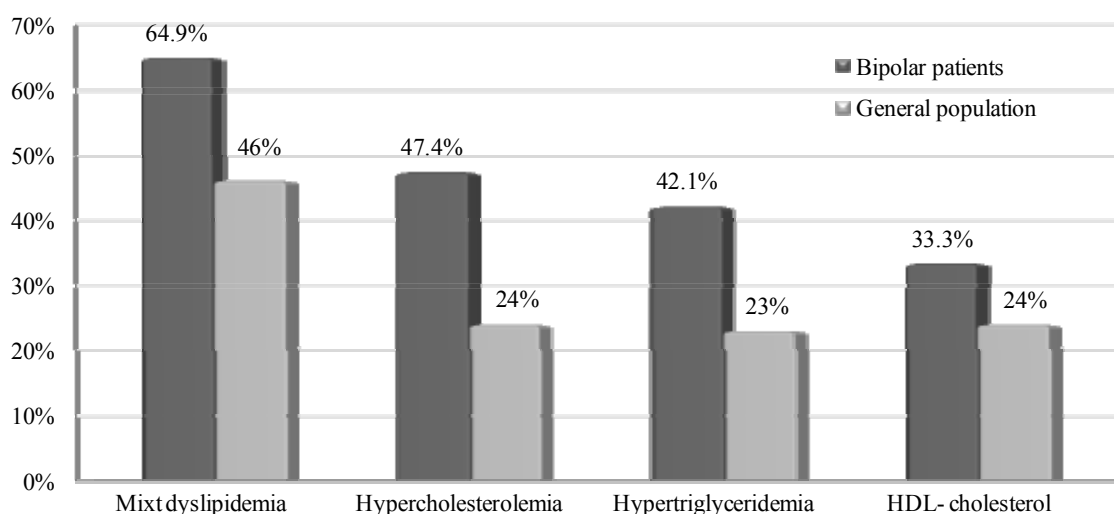


Fig. 4: *Distribution of patients according to lipid profile*

Chronic spinal pain was found at 36.84 % of bipolar patients. Of these, 15.8 % of patients were diagnosed with cervical spondylosis, and 21.05 % with lumbar spondylosis. Additional, 10.5 % of patients were diagnosed with gonarthrosis. These physical illnesses are associated with significant impairment and disability which have a tremendous impact on the patients' lives.

Obesity is defined as a body mass index (weight in kg divided by the square of height in meters) of $\geq 30 \text{ kg/m}^2$ and overweight as $25 - 29.9 \text{ kg/m}^2$. Obesity was present at 38.6 % of the patients, a 1.63 times higher percentage of the one found in the general population, and overweight was present at 21 % of the patients. (8)

Visceral obesity, measured by waist circumferences (> 102 cm in men and > 88 cm in women), was found at 66.7 % of the bipolar patients. Central obesity is associated with a statistically higher risk of heart disease, hypertension, insulin resistance, and diabetes mellitus type 2. The Na-

tional Cholesterol Education Program Adult Treatment Panel III suggested a cutting off of 102 cm for males and 88 cm for females, as a marker of central obesity, the same being used in defining metabolic syndrome. (5)

High rates of obesity among people with bipolar disorder can be attributed to poor diet and sedentary lifestyle, but drugs may also be a contributing factor, because antipsychotics can induce or exacerbate weight gain, and sedatives may increase inactivity in daytime sedation.

Type 2 diabetes was diagnosed according to American Diabetes Association 2003 criteria. (Tab. III) Type 2 diabetes was present in 10.5 % of patient and additional 15.8 % of patients met criteria for impaired fasting glucose, with higher rates than in the general population, 2.1 times higher and, respectively 1.2 times. (8, 10)

Tab. III: *Criteria used for glucometabolic classification according to ADA 2003*

Glucometabolic category	Classification criteria mmol/L (mg/dL)
Normal glucose regulation (NGR)	FPG < 5.6 (100)
Impaired fasting glucose	FPG ≥ 5.6 (100) and < 7.0 (126)
Diabetes mellitus (DM)	FPG ≥ 7.0 (126)

Values are expressed as venous plasma glucose.

FPG = fasting plasma glucose.

Among patients with diabetes, 66.7 % received hypoglycemic treatment (either oral antidiabetics or insulin). However, the control of glycemia in diabetic subjects was poor: 75 % had hyperglycemia. The prevalence of visceral obesity was higher in patients with hyperglycemia than in the remaining patients (59 % vs. 30 %). (Fig. 5)

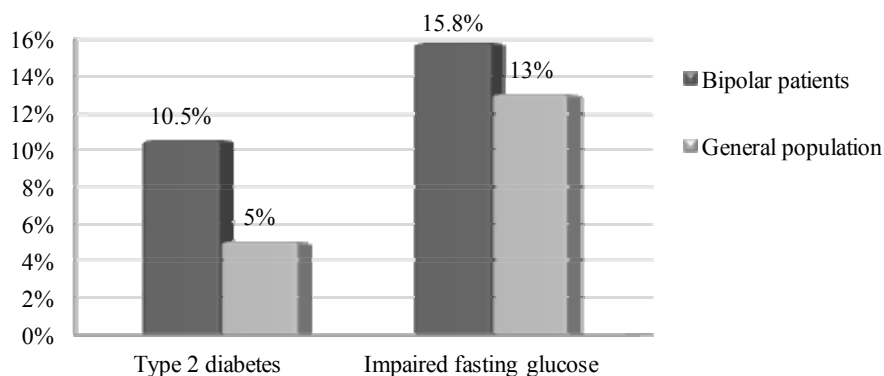


Fig. 5: *Distribution of patients according to glycemic profile*

Metabolic syndrome, defined as a cluster of metabolic, hemodynamic and anthropometric disturbances, is a predictive factor of type 2 diabetes and cardiovascular diseases. Among the essential criteria of the metabolic syndrome, according to WHO, insulin resistance and estimating consumption of insulin or its substitutes have an important role. (9)

The USA National Program of Education on Cholesterol is proposing a simplified definition for clinical practice, not including insulin resistance. Thus, people with metabolic syndrome should meet three of the following criteria:

- elevated blood pressure (> 130/85 mmHg);
- high plasma levels of fasting glucose (> 6.1 mmol/l or > 110 mg/dl);
- abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women);

- low serum concentrations of HDL-cholesterol (< 1.04 mmol/l in men and < 1.29 mmol/l in women);
- elevated serum levels of triglycerides (> 1.69 mmol/l). (5)

Metabolic syndrome criteria were met in 52.3 % of the patients. The percentage of individuals meeting the criterion for metabolic syndrome was higher than the rate reported in the NHANES survey (40.8 %). Many components of the metabolic syndrome are associated with a sedentary life-style, including increased adipose tissue (predominantly central); reduced HDL cholesterol, and a trend toward increased triglycerides, blood pressure, and glucose in the genetically susceptible patients. Medication may be a contributing factor, because antipsychotics can induce metabolic disorders. (11)

CONCLUSIONS

Bipolar disorders are associated with a substantial chronic medical burden. The familiarity with conditions affecting this population may assist in programs aimed at providing medical care for the chronically mentally ill.

There are several causal pathways that may be salient to the overlap between bipolar disorder and medical comorbidity. Patients with bipolar disorder display many risk factors for general medical disorders, such as insufficient access to primary and preventive health care, lower socioeconomic status, poor adherence to medical regimens, smoking, habitual inactivity, substance abuse, and high caloric intake. Patients with bipolar disorder are at elevated risk for each of these types of behaviours which raise their risk of developing a chronic illnesses and having poor medical outcomes, once the illnesses emerge. Iatrogenic causes are also possible; that is, medications for the management of bipolar disorder have a panoply of adverse effects on the physical health – for example, hypothyroidism (lithium), diabetes mellitus type 2 (second-generation antipsychotics).

Recognition of comorbidity in bipolar disorder is a very important element in the psychiatric practice. Patients with bipolar disorder often suffer from abdominal obesity, hypertension, hyperglycemia and hypertriglyceridemia, all characteristic of metabolic syndrome. Metabolic status should be monitored when initiating and changing antipsychotic medication. Psychiatrists need to assume responsibility for monitoring and lifestyle counselling, including education about healthy habits, especially when prescribing medications which may increase the metabolic complications.

Almost half of patients experience chronic pain that is associated with significant impairment and disability, which has a tremendous impact on patients' lives.

Chronic medical disorders were associated with a more severe course of bipolar disorder, increased household and work maladjustment, receipt of disability payments, reduced employment, and more frequent medical service utilization.

ACKNOWLEDGMENTS AND DISCLOSURE

The authors declare that they have no potential conflicts of interest to disclose.

REFERENCES:

1. Kupfer, D. J. Epidemiology and clinical course of bipolar disorder: Bipolar Disorder: The Clinician's Reference Guide. Montvale, NJ: Clinical Psychiatry LLC; 2004.
2. Jules Angst *et al.* Toward a re-definition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders and hypomania, Journal of Affective Disorders, Volume 73, Issues 1 – 2, January 2003, Pages 133 – 146.
3. Martinez-Aran, A. *et al.* Functional outcome in bipolar disorder: the role of clinical and cognitive factors, Bipolar Disorders 2007; 9(1-2): 103–113.
4. Goodwin, G. M. Evidence-based guidelines for treating bipolar disorder: revised second edition – recommendations from the British Association for Psychopharmacology, Journal of Psychopharmacology, 2009;23:1–43.
5. Gotheffors, Dan M. D. *et al.* Swedish clinical guidelines – Prevention and management of metabolic risk in patients with severe psychiatric disorders, 2010, 64: 5, Pages 294 – 302.

6. Correll, C. U., Manu, P., Olshanskiy, V., Napolitano, B., Kane, J. M., Malhotra, A. K. Cardiometabolic risk of second generation antipsychotic medications during first-time use in children and adolescents. *JAMA* 2009;302:1765 – 73.
7. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. Third Report of the National Cholesterol Education Program (Adult Treatment Panel 3). *Circulation* 2002; 106:3143 – 421.
8. Ford, E. S., Giles, W. H., Dietz, W. H. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA* 2002; 287: 356 – 359.
9. Dorobanțu, M. *et al.* Prevalence, Awareness, Treatment, and Control of Hypertension in Romania: Results of the SEPHAR Study, *International Journal of Hypertension*, 2010:970694.
10. Guidelines for the Management of Arterial Hypertension The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC), *Journal of Hypertension* 2007, 25:1105 – 1187.
11. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases, 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), *European Heart Journal* 2007, 28:88 – 136.