

## IMPACT OF METABOLIC STATUS ON THE COURSE OF ATRIAL FIBRILLATION

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### Abstract

**Background and aims:** Metabolic syndrome (MS) might influence the course of atrial fibrillation (AF) similarly to diabetes (DM). Aim of this research is to evaluate the quality of life, disease burden and medication adherence of patients with different metabolic states. **Material and methods:** A cross-sectional study of Latvian Center of Cardiology Arrhythmology Department patients with AF, sorting patients in 3 categories according to the National Institutes for Health guidelines criteria for MS. **Results:** From 133 patients, 51 were in metabolically healthy (MH) group, 58 in MS group and 24 had DM. Average age was 62.59 in MH, 67.59 in MS and 66.25 in DM group. Most common form of AF was persistent - MH 49%, MS 65.5%, DM 75%. Best EHRA median value was observed in DM group (29.2% reporting mild symptoms). Majority of patients had 1-2 comorbidities in MH and MS group and 3-5 in the DM group, with almost all patients using 4-9 drugs daily. **Conclusions:** A similar course of AF was observed in MS and DM groups. Since the same molecular pathways are involved, MS should be viewed as a cluster of risk factors with a cumulative effect - greater than the effect of a single risk factor.

**key words:** diabetes mellitus, atrial fibrillation, obesity, metabolic syndrome

### Background and aims

There is a proven link between diabetes and atrial fibrillation susceptibility [1,2] bringing up the question if other changes in metabolic status such as metabolic syndrome are capable of influencing the susceptibility, course, treatment and outcome of atrial fibrillation. Criteria for metabolic syndrome, as defined by National Institutes for Health guidelines, [3] - hypertension, obesity, decreased levels of high density lipo cholesterol, elevated triglycerides and elevated blood sugar - are known risk factors

for atrial fibrillation [4], but most of them are studied separately instead of a cluster as they appear in the case of metabolic syndrome. Which could be very likely generating a cumulative effect. With the growing prevalence of metabolic syndrome - ranging from 24% of population in continental Europe [5] to 78% in northern Europe [6] - and atrial fibrillation already affecting around 2% of Europe [6], this connection should be thoroughly investigated. This might prove crucial for understanding and treating atrial fibrillation - an illness that is predicted to become more prevalent in the aging

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European population [7], especially considering advances in our ability to treat cardiac and other chronic diseases.

Existing data on the association between the two is lacking and often contradictory with some studies reporting twice the prevalence of atrial fibrillation in patients with metabolic syndrome compared to patients without [8], yet some researchers remain unconvinced [9]. This research looks at and compares the quality of life, disease burden, lifestyle and medication adherence of patients with different metabolic status.

## **Material and methods**

### *Study design and patients*

This was a cross-sectional study of Latvian Center of Cardiology Arrhythmology Department patients who had a confirmed diagnosis of atrial fibrillation at the time of study. Patients were sorted into 3 categories - metabolically healthy or MH (excluding patients with uncontrolled thyroid issues), with metabolic syndrome or MS and patients with confirmed diagnosis of diabetes or DM, without a further division of patients with type 1 or type 2 diabetes. Patients, with the help of an assistant available for clarifying unclear questions, were asked to fill in a questionnaire regarding their quality of life, disease burden, lifestyle and medication adherence.

### *Laboratory, anthropometric and clinical data collection*

Data on medication, polymorbidity and blood analysis was collected from medical histories. An assistant carried out measurements of patients with a calibrated scale, subtracting weight of the clothing a patient was wearing. Waist measurement was taken without clothing, leveling the tape at the belly button and reading the measurement after an exhale. BMI was

calculated by dividing weight in kilograms by the square of the height in meters. Patients were grouped in the category of metabolic syndrome if their waist circumference exceeded 89 cm for women and 102 cm for men, triglyceride levels at or above 1.7 millimoles per liter, high density lipo cholesterol below 1.3 millimoles per liter for women and 1.04 for men, blood pressure above 130/85 mmHg, blood fasting sugar above 5.6 millimoles per liter or if a patient was taking medication to control any of these traits.

### *Statistical analysis*

SPSS version 22.0 was utilized for the data analysis. P value was considered significant at <0.05. One-way ANOVA was used to compare means of the groups and Pearson's chi-square test for categorical data evaluation.

## **Results**

Baseline characteristics of the 133 patients can be found in [Table 1](#). 51 were in MH group, 58 in MS group and 24 had DM. 44% of the participants were women, the mean age of participants being 64.4 years. There was a similar number of smokers in all groups, removing smoking as a possible influencer of results. 22 of all the patients were acutely admitted for hospitalization at the time of the study

Blood pressure analysis reported 27.5% patients with hypertension in MH group, 37.9% in MS group and 48% in DM group. However, the average systolic and diastolic blood pressures in each group were similar ranging from 145/94 mmHg in MH group to 149/90 mmHg in the DM group.

Laboratory findings can be found in [Table 2](#). Highest average fasting blood glucose was reported in DM group at 8.28 mmol/l, metabolically healthy group reported normal average blood glucose levels. Average cholesterol and LDLH were found in

metabolically healthy group, however they also had the highest levels of HDLH and lowest levels or triglycerides.

**Table 1.** Baseline characteristics. A comparison of patient baseline characteristics between all groups showing average age, number of female patients, average BMI, number of smokers, number of patients admitted in acute care.

	Metabolically healthy	Metabolic syndrome	Diabetes Mellitus	All
Age	62.5	67.5	66.2	64.4
Female sex (n)	24	26	8	58
Average BMI	26.7	31.9	36.9	30.8
Smoker (n)	4	5	2	11
Acute care (n)	12	7	3	22

**Table 2.** Laboratory findings. A comparison of the average glucose, cholesterol, high density lipocholesterol (HDLH), low density lipocholesterol (LDLH), triglycerides between the groups of metabolically healthy, metabolic syndrome and diabetes mellitus patients.

mmol/l	Metabolically healthy	Metabolic syndrome	Diabetes Mellitus
Average glucose	5	6.17	8.28
Average cholesterol	5.16	4.43	4.32
HDLH	1.44	1.27	1.33
LDLD	3.2	2.5	2.32
Triglycerides	1.28	1.63	1.84

**Table 3.** Life quality measures. A comparison of life quality markers between the groups of metabolically healthy, metabolic syndrome and diabetes mellitus patients, showing percentage of persistent atrial fibrillation, number of patients with low medication adherence, percentage of patients with high life quality, average EHRA score, average number of polymorbidities and drugs used daily.

	Metabolically healthy	Metabolic syndrome	Diabetes Mellitus
Persistent atrial fibrillation (%)	49	65.5	75
Low medication adherence (n)	4	3	3
High life quality (%)	5.9	15.5	29.2
EHRA score	2.65	2.52	2.42
Average polymorbidities (n)	2.22	2.59	3.96
Average drugs used daily (n)	3.76	4.38	7.25

Life quality assessment can be found in table 3. Most common form of atrial fibrillation was persistent - MH 49%, MS 65.5%, DM 75%, with MH having the highest incidence of permanent AF (7.8%) (p=0.221). There was a similar number of patients with self-reported low medication adherence in all groups. The lowest average life quality and highest EHRA score was reported by the MH group, with only 5.9% of the group reporting high life quality. Average number of polymorbidities and drugs used daily was the highest in the DM group.

### Discussions

This study showed that subjects meeting the criteria for metabolic syndrome were more prone to complicated course of atrial fibrillation with more cases of persistent atrial fibrillation, higher number of drugs used daily and more comorbidities.

Type 2 diabetes is an established risk factor for atrial fibrillation and some knowledge has been gathered on the potential molecular mechanisms at play responsible for this association [10]. One has to recognize that metabolic syndrome also would utilize the same molecular pathways, triggering the same cascade [11].

More research is needed to establish a difference in risk for developing atrial fibrillation between patients presenting a single risk factor for example high blood pressure versus patients with metabolic syndrome. In our study the metabolically healthy group was defined as individuals who did not meet necessary number of criteria to classify them as having metabolic syndrome, did not have diabetes mellitus or thyroid dysfunction, however most of these patients had either high blood pressure or elevated triglycerides, or low density lipo cholesterol. Since even the metabolically healthy group usually presented

with at least one risk factor for atrial fibrillation [4,12], our study has observed that a cluster of risk factors in the case of metabolic syndrome should be looked at as more dangerous than just a single risk factor because of its cumulative effect.

Our study had some limitations - the quality of life and disease burden were self-reported, creating a paradox with metabolically healthy people with few comorbidities reporting a lower overall life quality than patients with diabetes who had a much higher count of comorbidities, were much more likely to have persistent atrial fibrillation and often presented with heart failure. This paradox has been observed in other studies too [13], the Finnish Twin Cohort found that life satisfaction was not always associated with mortality, meaning that otherwise healthy adults might rate their symptoms as more alarming and burdening than patients who are already used to burden of other diseases.

### Conclusions

Overall patients with MS fared worse than MH group, but better than patients with DM, showing a correlation between MS and a more complicated course of AF similar to that associated with DM. Physicians should be aware of this when treating a patient with atrial fibrillation, as it might influence the course, outcome and overall patient satisfaction with the received treatment. Diabetes mellitus and metabolic syndrome increase the risk of atrial fibrillation through the same molecular pathways and should be viewed as a cluster of risk factors with a cumulative effect which is far greater than the effect of a single risk factor.

Caution must be used in assessing the disease burden, because patients presenting with other morbidities might under-report their symptoms and vice versa.

Further studies are needed to understand the mechanisms at play and to establish other possible high-risk groups when it comes to atrial fibrillation.

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