



# ATRIAL FIBRILLATION IN PATIENT WITH TYPE-2 DIABETES MELLITUS: FROM CAUSES TO CLINICAL PRACTICE

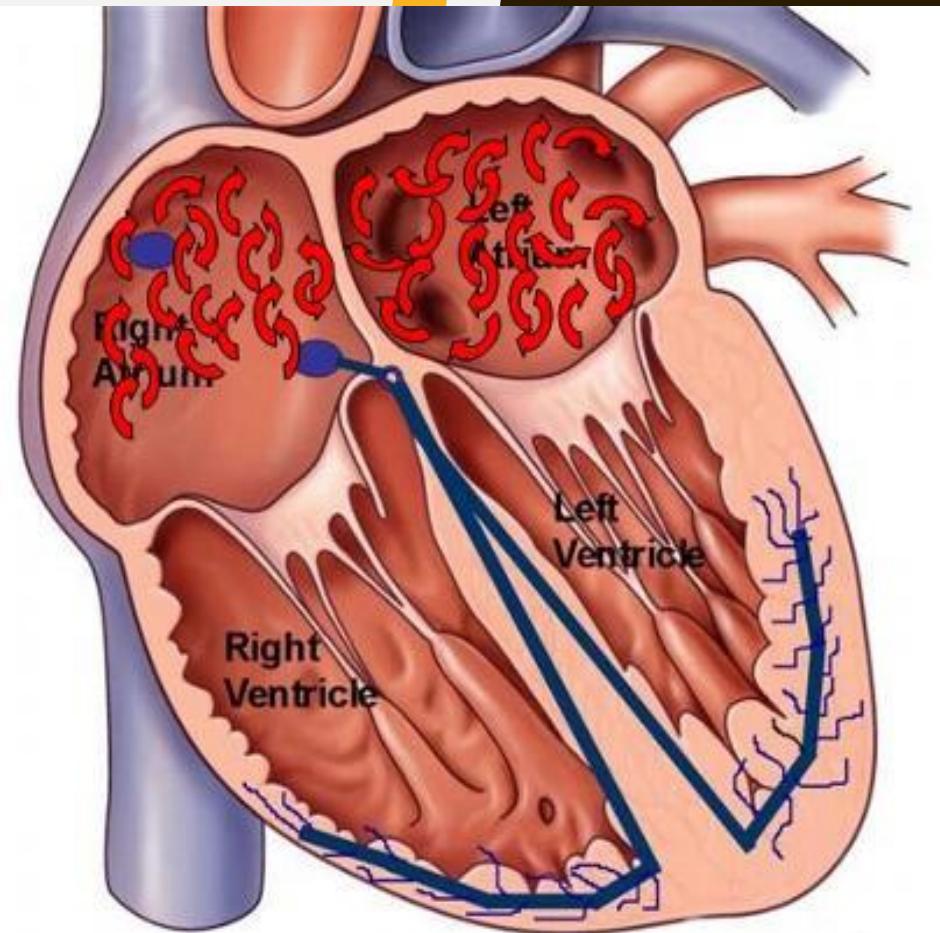
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**Atrial fibrillation (AF) is the most frequently encountered cardiac arrhythmia** in clinical practice. AF is strongly age-dependent, affecting 4% of individuals older than 60 years and 8% of persons older than 80 years. It is estimated that its prevalence will increase by 2.5 fold by the year 2050.

<https://emedicine.medscape.com/article/151066-overview>

At the same time, **diabetes mellitus (DM) has become a widespread disease**. It is estimated that by 2035, the number of patients with diabetes will have risen to 592 millions.

Archives of Cardiovasc Disease. Volume 108, issue 4, 2015

**DM and AF share common precursors such as hypertension, atherosclerosis, and obesity, and are marked predictors for stroke and mortality**. It is unclear if this is a direct causal one, or if there are other indirect interactions between the conditions, and the mechanism of this link remains uncertain. The duration of diabetes and a higher HbA1c are also linked to a greater risk of AF.

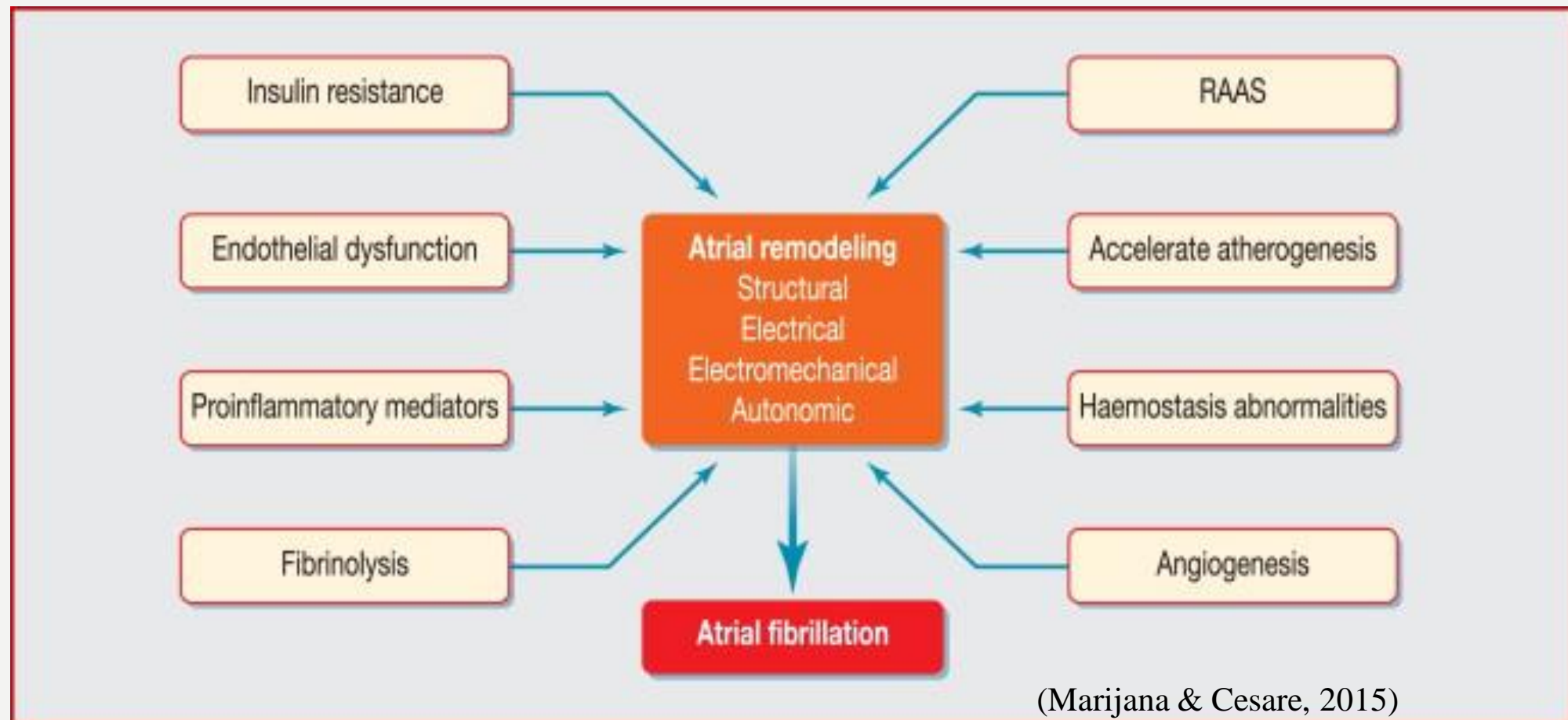
Cardiovasc Dis Res. V.1(1), Jan-Mar 2010

Studies have shown that DM is frequently associated with AF, it is however difficult to determine whether DM directly affects atrial tissue or whether different pathways are involved, including hypertension (HT), coronary artery disease (CAD), and abnormal activity of the autonomic nervous system.

Archives of Cardiovasc Disease. Volume 108, issue 4, 2015

## Mechanisms of the relationship between diabetes and AF

Insulin resistance, impaired glucose tolerance, pro-inflammatory mediators, abnormalities of hemostasis, fibrinolysis, angiogenesis and extracellular matrix turnover are metabolic defects commonly associated with DM. These metabolic changes lead to endothelial dysfunction, abnormal activation of the renin-angiotensin-aldosterone system and acceleration of atherogenesis, which could be responsible for AF occurrence. Diabetes could also cause structural, electrical, electromechanical and autonomic remodeling.



# OUR PATIENT

- Patient B.A.S
- Age: 78 y. old
- Gender: female
- On pension
- City resident

# COMPLAINTS

- palpitation
- episodic pain in left part of chest, pressing character, no clear connection with provoking factors.
- dyspnea on mild physical exertion
- labile blood pressure

# ANAMNESIS MORBI

patient has a 2-year history of arterial hypertension and atrial fibrillation with a blood pressure (BP) of 170/100mmHg, which was unsuccessfully ambulatory treated with amiodarone, digoxin, aspirin, spironolactone, and lisinopril. Hyperglycemia-during several years, not treated, diagnosis DM wasn't established on account of medical observation luck. She was admitted to the hospital following a deterioration in her health due to unsuccessful previous therapy.

# ANAMNESIS VITAE

- Past medical history:
  - Pneumonia 5 years ago
  - Chronic bronchitis 10 years ago
  - Deforming gonarthrosis and coxarthrosis for 15 years
- Family history of DM and cardiovascular disease: mother had DM
- Allergic history: allergic dermatitis for digoxin
- Social history: doesn't smoke or abuse alcohol
- Childhood infections: none

# OBJECTIVE STATUS

- Consciousness: clear; state: moderate severity; body position: active. Temperature: 36.7C
- Patient can orientate herself in place, time and personality. Moves with a walker only.
- **Appearance: pale skin, acrocyanosis. Dermatitis of both palms on previous digoxin treatment.**
- Thyroid gland: cannot be palpated
- Musculoskeletal: deformation of hip and knee joints, patient can only walk with support
- **Obesity II degree (BMI - 35.0)**
- Respiratory rate- 22/min.;
- Lung percussion: no clinically significant changes, resonance
- Lung auscultation: weakened breathing in the lower parts of both lungs
- Pulse: **arrhythmic, 90 bpm**; BP - **160/80 mmHg**
- Borders of the heart: **left border is displaced 2cm outwards from the left mid clavicular line.**
- Heart auscultation: **heart rate- 97/min, arrhythmic, atrial fibrillation. Muffled heart tones, accentuation of the second tone on the pulmonary trunk point of auscultation, diffuse systolic murmur in all points with epicenter at the apex of the heart.**
- Abdomen: soft and painless, enlarged due to deposition of adipose tissue.
- Liver: near the rib edge, no pain on palpation of the right hypochondriac region. Spleen: not palpated
- Pasternatsky symptom: negative on both sides.
- Stool and diuresis: normal
- **Bilateral pitting edema of lower extremities**



# COMPLETE BLOOD COUNT

	results	normal range
Hemoglobin	152	120-140g/l
Red blood cells *10 <sup>12</sup>	5.06	3.9-4.7
Hematocrit, %	43.0	36 - 42
Leukocytes *10 <sup>9</sup>	7.3	4.0-9.0
Neutrophils: bands	1%	1.06-6.0%
Neutrophils: segmented	68%	47.0-72.0%
Eosinophils	9%	0.5-5.0%
Basophils	1%	0-1%
Lymphocytes	15%	19.0-37.0%
Monocytes	6%	3.0-11.0%
Thrombocytes *10 <sup>9</sup>	245	180-320
ESR, mm/h	13	2-15mm/h

**Conclusion:** increase of hemoglobin level, erythrocytosis, eosinophilia

# URINE TEST

	28.03.18	N
$\rho$	1.030	1.001 – 1.040
glucose	-	-
protein	0.03	- , g/l
WBC	½ of field	1-2
hyaline casts	1-2	-
granular casts	-	-
pH	5,5	5-7
RBC	10-12	0
other	bacterias, many uric acid crystals	- -

Conclusion: microalbuminuria, hematuria as signs of diabetic nephropathy;  
leukocyturia, bacterias

# BIOCHEMICAL BLOOD ANALYSIS

	result	normal range
Glucose (mmol/l)	7.23	3.9 - 6.4
Total bilirubin (mkmol/l)	15.4	1.7 - 21.0
AST (U/l)	18.3	Till 31
ALT (U/l)	11.4	Till 31
Creatinine (mkmol/l)	94	44 - 80
GFR, (mL/min)	79.42	> 90
TSH (mk ME/ml)	3.13	0.25 - 5

**Conclusion:** hyperglycemia (DM 2 type), hypercreatinemia, low GFR (diabetic nephropathy)

# GLYCEMIC PROFILE

blood glucose 01-march-2018	result (mmol/l)	Normal range (mmol/l)
8-00	5.1	3.9 - 6.4
11-00	5.8	3.9 - 6.4
14-00	5.5	3.9 - 6.4
17-00	10.7	3.9 - 6.4
20-00	4.6	3.9 - 6.4
23-00	6.2	3.9 - 6.4

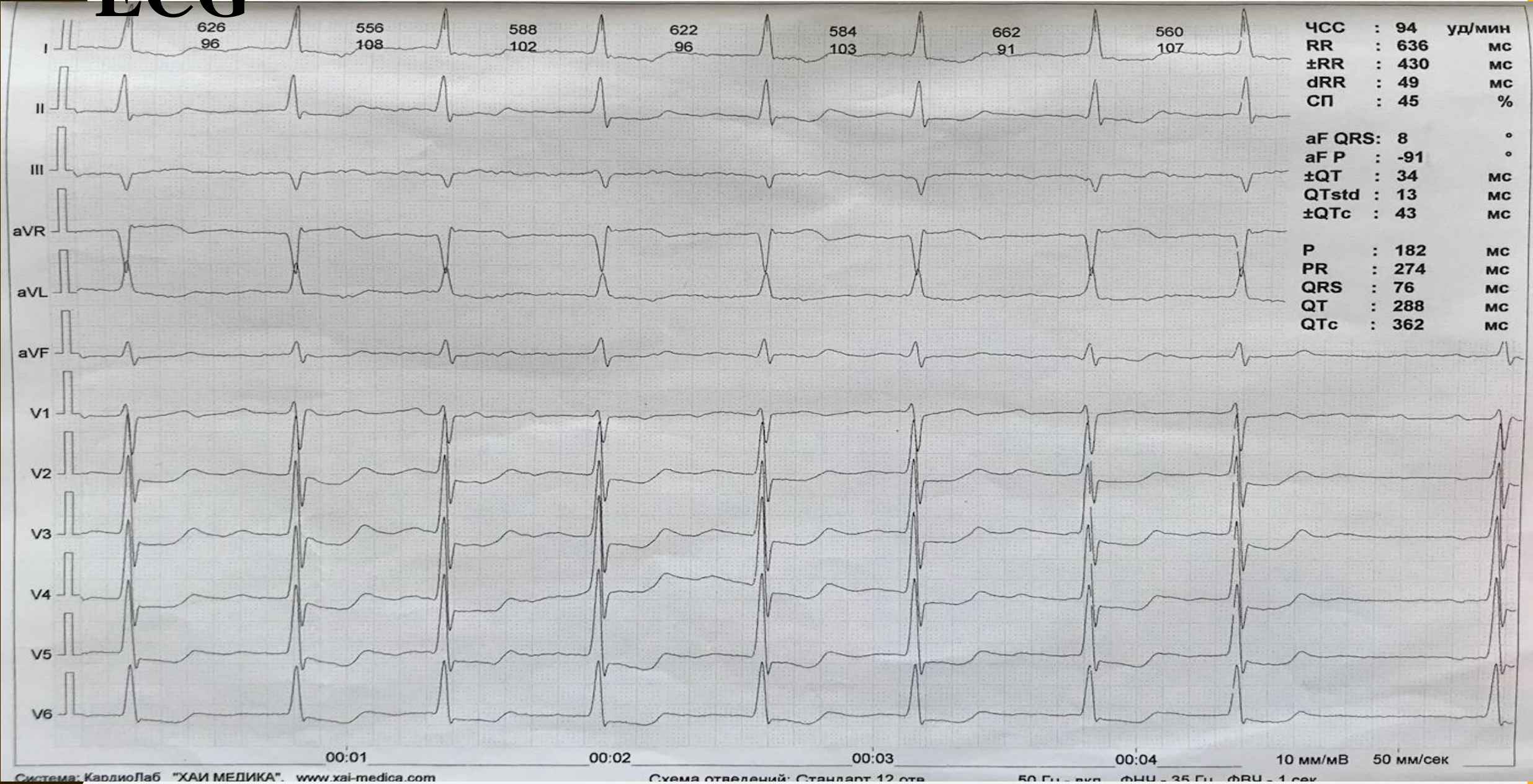
**Conclusion:** fasting plasma glucose level is under control due to effective diabetic therapy with metformin (except lunch time at 17-00, patient ate white bread during lunch), adjustment of dose was made

# LIPID PROFILE

28 –march-2018	result (mmol/l)	normal range
Total cholesterol	5.66	< 5.2
VLDL cholesterol	0.52	<1.0
LDL cholesterol	4.05	<3.5
HDL cholesterol	1.08	> 0.9
Triglycerides	1.17	<2.3
Index of atherogenicity	4.24	till 3.0

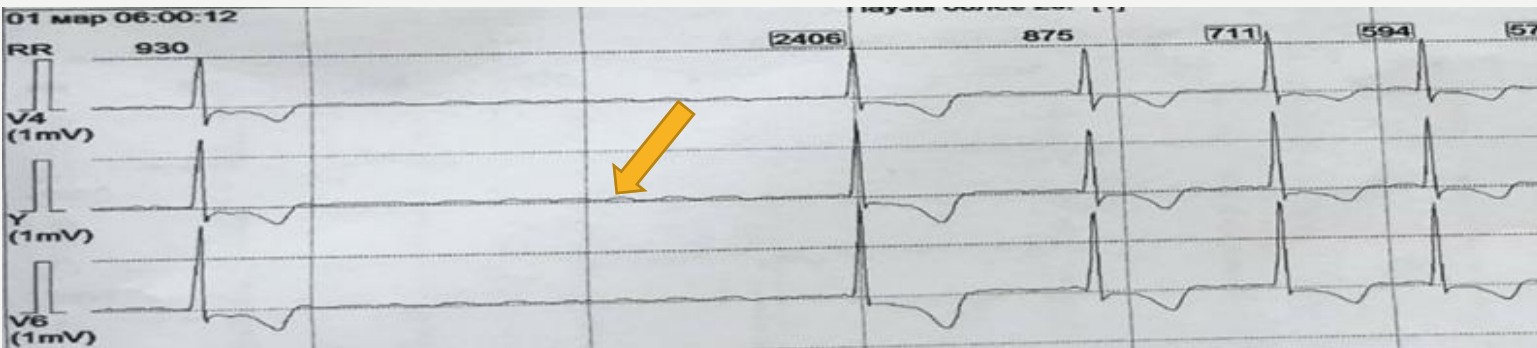
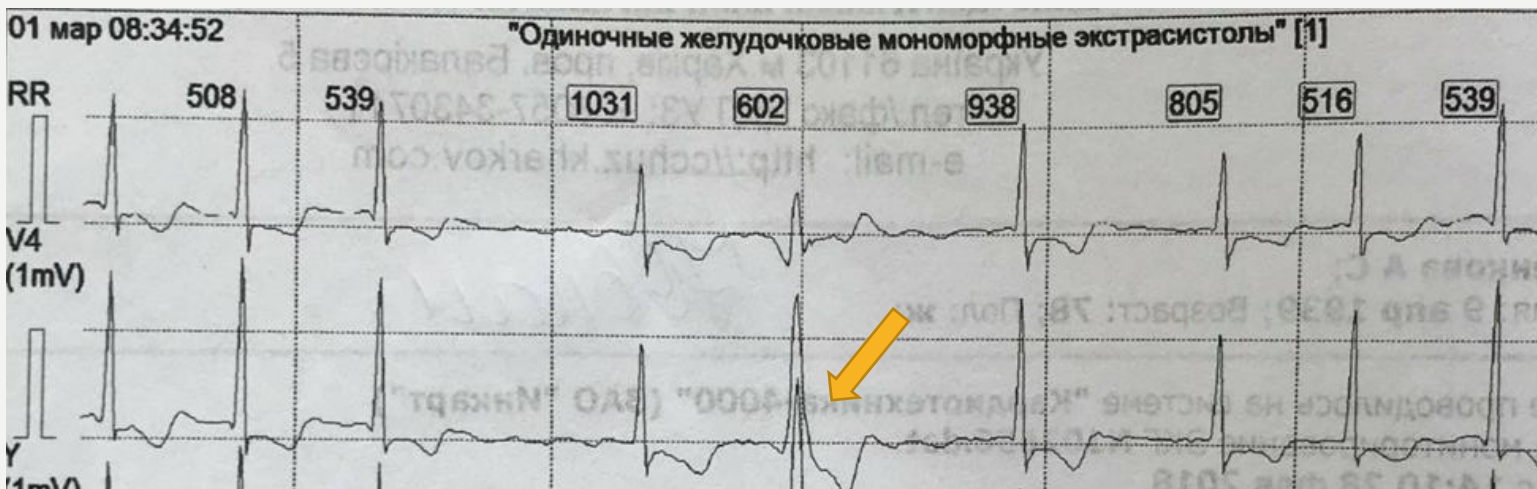
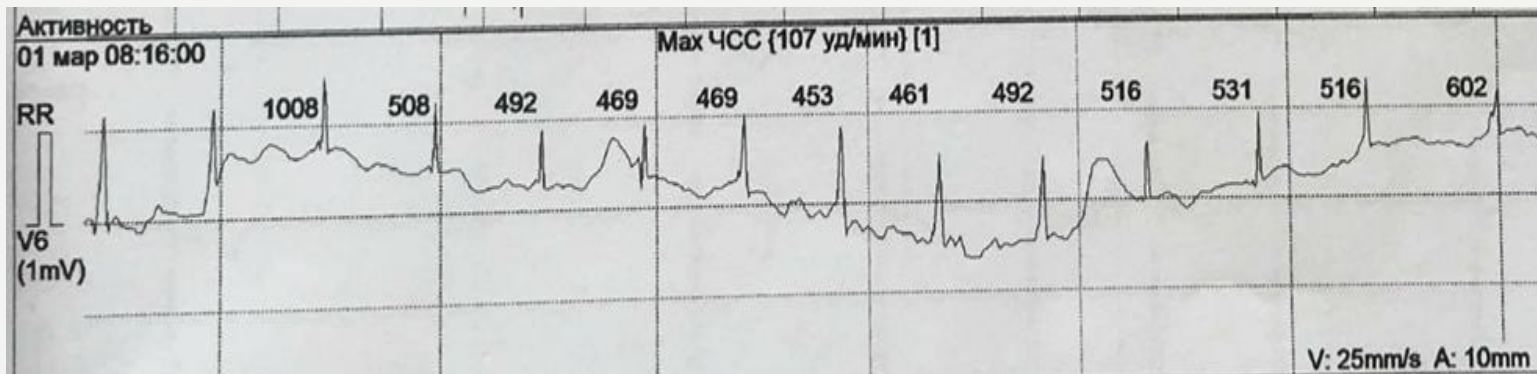
Conclusion: dyslipidemia

# ECG



**Conclusion:** atrial fibrillation, LV myocardium hypertrophy, alternation of repolarization as ST-depression in V2-V6, I,II -1mm

# 24-hour ECG monitoring 01-march-2018



**Conclusion:** Circadian index - 104%, atrial fibrillation with HR from 56 to 107/min. (mean 74). Single ventricular extrasystoles with a pre-test interval of 602ms. During the day: 1 (less than 1 per hour). At night: none. Pauses more than 2s. With a pre-test interval from 2000 to 2406msec. Total: 17 (1/hour). Day: 9 (1 per hour). At night: 8 (1 per hour). Abnormal repolarization of left wall of the heart.

# CHEST X-RAY

- No focal infiltrates or shadows in lungs
- **Signs of pulmonary hypertension:** enlarged pulmonary arteries, enlarged right atrium, elevated cardiac apex due to right ventricular hypertrophy.
- Lung roots are normal
- Sinuses are free. Diaphragm – normal.
- **Enlargement of heart shadow to the left**
- **Sclerotic changes of the aortic arch**
- Widening of the upper mediastinum to the right side





# ECHOCARDIOGRAPHY

Aorta: d 32,2 cm, sclerotic changes of aortic walls, dilatation of the ascending aorta, fibrosis and calcinosis of aortic valve, aortic regurgitation –I-II degree

Tricuspid valve – regurgitation I-II degree. Pulmonary trunk valve – regurgitation I stage.

Pressure in pulmonary trunk is 38,7 mm Hg (n < 15).

Mitral valve – cuspids are moderately thickened, fibrosis and calcinosis, regurgitation II-III degree.

EF – 54% (N - 55 – 78%). FC – 28% (N - 28 – 44%).

*Left Ventricle:*

FDD – 48,9 mm (N – 35 – 55mm)

FSD – 35,1 mm (N – 23 – 38 mm)

Posterior wall thickness in systole– 16,6 mm (N – 6 – 11mm).

Intraventricular septum size in diastole– 16,2 mm ( 6 – 11 mm)

*Right Ventricle:*

Diameter – 31,9 mm (N – 9 – 26 mm)

Wall thickness – 6,9 mm (N – 3 - 6 mm).

*Left atrium* – enlarged – 44,1 mm in diameter ( N – till 38 mm)

*Right atrium* – enlarged, 48,8 mm (N – 21-37).

Intraatrial septum – not changed, no defects.

**Conclusion:** Atrial fibrillation, sclerotic changes of aorta, dilatation of the ascending aorta. Aortic regurgitation I-II degree. Mitral regurgitation II-III degree. Tricuspid regurgitation II degree. Pulmonary trunk regurgitation I stage. Moderate dilation of right and left atriums. Myocardial hypertrophy of both ventricles. Pulmonary hypertension II stage.

# ABDOMINAL ULTRASOUND

- Diffuse change of liver parenchyma with mild hepatomegaly
- Congestive process in portal vein system
- Cholestasis of gall bladder
- Chronic non-calculous cholecystitis
- Diffuse changes of pancreatic parenchyma
- Kidney calcinosis
- Diffuse changes of both kidneys parenchyma
- Right kidney cyst and pyeloectasia

# COMPLETE DIAGNOSIS

## *Main:*

Coronary artery disease: stable angina III functional class.

Arterial hypertension stage 3, III degree.

Permanent atrial fibrillation.

CHA2DS2-VASc score 5 points. HAS-BLED Score 2 points. ATRIA Bleeding Risk Score 3 points.

Chronic heart failure stage IIIC with preserved ejection fraction, III functional class by NYHA.

Type 2 diabetes mellitus, complicated by diabetic nephropathy stage 2 (incipient nephropathy).

Chronic Kidney Disease stage 2 (GFR - 79.42 mL/min)

## *Concomitant diseases:*

Chronic non calculous cholecystitis. Chronic pancreatitis. Deforming bilateral gonarthrosis and coxarthrosis.

# TREATMENT OF OUR PATIENT

- **Goals of treatment include:** rate control  
dyslipidemia and hyperglycemia control,  
tromboembolism prevention  
treatment of comorbid conditions.
- **Prescribed Medications:**
  - Clopidogrel 75mg 1 time/day
  - Nebivolol 5mg 1 time/day
  - Valsartan 80mg 1 time/day
  - Atorvastatin 80mg 1 time/day
  - Torasemide 10mg 1 time/day
  - Cardioarginin 5ml IV 1time/day for 5 days.
  - Metformine initial -500mg PO every 12 hr, after adjustment: 1500mg/day.

# RECOMMENDATIONS

- Lenient rate control (<110 beats per minute resting) is recommended over strict rate control (<80 beats per minute resting) for patients who have atrial fibrillation. Rate control is recommended in preference to rhythm control for the majority of patients who have atrial fibrillation. Preferred options for rate control therapy include non-dihydropyridine calcium channel blockers (contra-indicated in LV failure with pulmonary congestion) and beta blockers.
- Chronic anticoagulation is recommended for patients who have atrial fibrillation unless they are at low risk of stroke (CHADS<sub>2</sub> <2) or have specific contraindications (strong recommendation, high quality evidence). Choice of anticoagulation therapy should be based on patient preferences and patient history. Direct thrombin inhibitors (dabigatran) and direct factor Xa inhibitors (apixaban, rivaroxaban, edoxaban and betrixaban), have been reported to have much better pharmacokinetic profiles, and to be more effective and safer than vitamin K antagonists in reducing stroke and embolic events or major bleeding in diabetic patients with AF. Dual treatment with anticoagulant and antiplatelet therapy is *not* recommended in most patients who have atrial fibrillation.
- Treatment with metformin seems to be associated with a decreased long-term risk of AF in diabetic patients and may even be associated with a lower long-term stroke risk, also for patient with established atherosclerotic cardiovascular disease therapy should begin with lifestyle management and metformin (+ in future empagliflozin and liraglutide, canagliflozin if needed proven to reduce major adverse cardiovascular events). Behavioral therapy designed to achieve >5% weight loss should be prescribed. Glycated haemoglobin and fasting glucose levels control once a half a year required.
- Special attention should be directed to reversion of atrial remodelling in diabetic patients with AF. Probucol, a lipid-lowering drug with a potent antioxidant effect has been proposed to positively influence atrial remodelling in AF.
- In adults with DM and hypertension, also in case of HFpEF and persistent hypertension antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher with a treatment DBP: goal of less than 130/80 mm Hg. Drugs of choice are ACE inhibitors and ARBs which also have the best efficacy among the drug classes on urinary albumin excretion.

# CONCLUSION

Atrial fibrillation and diabetes mellitus are common comorbid conditions, and the association between them has been proved both in epidemiology and experimental studies. These two conditions will be seen together more frequently in the future because the prevalence of both is on the rise. Therefore, it is very important to establish the most effective treatment in this subpopulation of patients with AF. New prospective studies with large numbers of patients with diabetes and AF are needed to investigate the mechanisms of this relationship and all possible therapeutic approaches in order to determine the best possible individual management of both conditions.

(Marijana & Cesare, 2015)

