Non-alcoholic fatty liver disease influence upon CAD course: two years follow-up prospective study

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Abstract

Objective of the study was to evaluate the influence of non-alcoholic fatty liver disease (NAFLD) upon CAD progression.

Materials and methods. Prospective 2 years follow-up in 315 patients after acute myocardial infarction and CABG was performed. All patients were divided into two groups: 1 – 214 patients (68%) with CAD and concomitant NAFLD (CAD+NAFLD); 2 – 101 patient (32%) CAD without NAFLD. Patients underwent clinical and instrumental examination, including contrast MSCT.

Results. Patients with NAFLD had poorer prognosis with more often grafts occlusion, worse CHF progression and cmore frequent significant ventricular arrhythmias. Patients with concomitant NAFLD have 1.5-fold higher risk of atrial fibrillation as CABG surgery complication. Also, patients with CAD+NAFLD have significantly higher total mortality within 2 years after CABG.

Conclusion. Concomitant NAFLD significantly worsens CAD flow after CABG.

Key words:

coronary artery disease, CABG surgery, non-alcoholic fatty liver disease, prognosis.

Over the past years there has been emerging numerous data regarding importance of non-alcoholic fatty liver disease (NAFLD) in cardiovascular patients with disseminated atherosclerosis, dyslipoproteinemia and metabolic syndrome (MS) [1,2,11]. Numerous studies prove that MS is strongly associated with elevated cardiovascular risk (CVR) [4,5,9,10], but according to recent studies results patients with NAFLD even without MS also have higher CVR [3,7,12]. Therefore, diagnosis and evaluation of NAFLD may be of use for CVR stratification.

Several studies witness for interconnection between atherosclerosis progression and NAFLD. Carmelo A. C., Gaspare M. P. et al. came to a conclusion that NAFLD, body mass index (BMI) and systolic blood pressure are independent markers of intima-media complex thickening in a a random sample of adolescents [3].

According to other study results multifactor analysis showed the following six markers to be very common in the patients with NAFLD: essential hypertension (odds ratio [OR] – 2,4; 95%, CI 1-5.6), diabetes mellitus (DM) type 2 (OR – 2,6; 95%, CI 1.1-6.3), sleep apnea (OR – 4,0; 95% CI 1.3-12.2), AST elevation >27 mmol/l (OR – 2,9; 95%, CI 1.2-7.0), ALT elevation >27 mmol/l (OR – 3,3; 95%, CI 1.4-8.0), being of not black race (OR – 8,4; 95%, CI 1.9-37.1) [7]. As a summary, according to Guilherme M. C., Kiran B., et. al NAFLD may be anticipated in obese individuals and patients with very high CVR [7]. Therefore, estimating the influence of co-existing NAFLD upon CAD progression is of significant importance due to high prevalence of hypertension and DM in the population.

Objective of the study was to evaluate the prognostic importance of NAFLD upon CAD progression over 2 years follow-up.

Materials and methods

Over 2 years we prospectively followed up 315 patients with CAD after acute myocardial infarction (AMI). We included patients planned for CABG surgery, receiving standard medication therapy as per existing guidelines (antiaggregants, statins, β-blockers, ACE inhibiors, nitrates in case of angina). Mean age constituted 43,8±10,2 yeas among 289 men (91%) and 26 women (9%). 255 (81%) of patients had essential hypertension. DM type 2 was diagnosed in 138 patients (43,8%). Angina pectoris was observed in 77,5% of the examined patients.

All patients underwent general examination, ECG, blood biochemistry analysis, ECG Holter monitoring, EchoCG, abdominal ultrasound (AUS), coronary angiography (CAG) and multi-spiral computed tomography (MSCT). MSCT with coronary contrasting wasperformed before surgery and 2 years after for grafts function evaluation. Diagnosis of NAFLD was established by determining the density of the liver parenchyma compared to spleen at MSCT.

Exclusion criteria were as follows: viral or alcoholic hepatitis history, hemodynamically significant valvular heart disease, COPD, history of myocarditis, transitory or persistent electric cardiac stimulation, acute heart failure, patients with implanted cardioverter-defibrillator.

Results and discussion

All patients according to examination results were divide into two groups. Group 1 included 214 (68%) patients, who were diagnosed to have CAD with concomitant NAFLD (CAD+NAFLD). Second control group included 101 (32%) patient with CAD without NAFLD. Groups were matched for pre-existing comorbidities, age and sex, as well as male and female distribution.

Group 1 was divided into two subgroups: a) patients with CAD and steatohepatitis (CAD+SH) (n=78, 25%); b) patients with CAD and steatohepatosis (CAD+H) (n=136, 43%).

Among subgroup 1a there were 50 (64%) patients with DM type 2 (16% from total amount of patients), and 28 patients (36%) with MS (9% from total amount of patients), respectively.

Among subgroup 1a there were 38 (28%) patients with DM type 2 (12% from total amount of patients), and 78 patients (57%) with MS (25% from total amount of patients), respectively. 20 (15%) patients from subgroup 1b had no MS (6% from total amount of patients). Subgroups characteristics is presented in Table 1.

According to our analysis result certain findings were significantly more often were observed in the patients with CAD+NAFLD. In the patients with CAD+NAFLD DM type 2 and MS are observed 3-fold more often compared to CAD patients without concomitant NAFLD (OR 3.05; 95%, CI 1.677 – 5.528; RR 2.301, p<0.0001; OR 2.99; 95%, CI 1.115 – 5.029; RR 2.001; p<0.0001, respectively). Also, patients with CAD+NAFLD 2 times more often were diagnosed with hypertension and obesity (BMI ≥30 kg/m2) (OR 1.8; 95%, CI 1.115 – 2.902; RR 1.358, p=0.016; OR 4.5; 95%, CI 2.663 – 7.342; RR 1.752; p<0.0001, respectively) (Fig. 1).

Our data shows that MS, insulin resistance, DM and increased body weigh which are major risk factors for NAFLD development, significantly more often co-exists with CAD and NAFLD combination, coinciding with Guilherme M.C., Kiran B., et. al. data, who showed that NAFLD mostly often is observed in the patients withhypertension, DM type 2, sleep apnea syndrome, serum transaminases elevation and being of not black race [8].

There were no cases of death during surgery or recurrent AMI as a complication of CABG surgery.

It is known that atrialfibrillation (AF) is one of the most frequent complications of CABG surgery. There were 78 (36.4%) cases of AF after surgery in group 1 (CAD+NAFLD, n=214), and 24 (23.7%) cases in

Table 1.
Group 1 (CAD+NAFLD) patients' characteristics

Comorbidities	CAD+SH			CAD+H		
	n	%	% from total amount of patients	N	N (%)	% from total amount of patients
DM type 2	50	64	16	38	28	12
MS	28	36	9	78	57	25
Without DM	0	0	0	20	15	6
Without MS	0	0	0	0	0	0

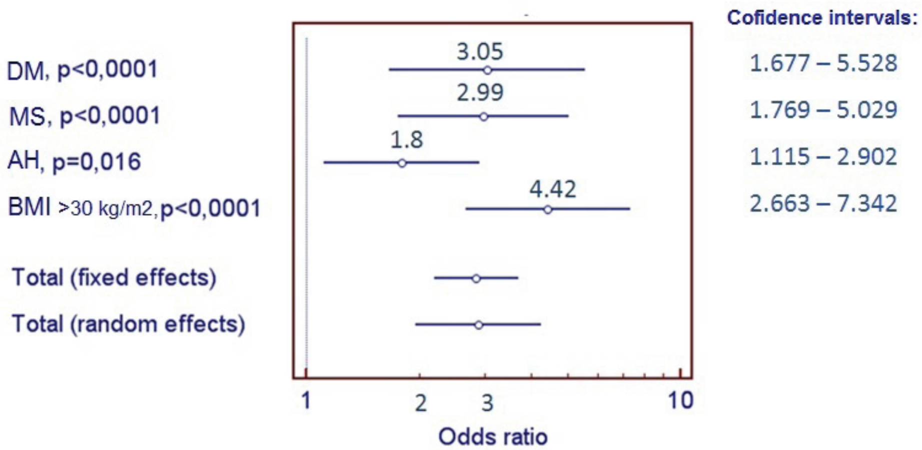

Fig. 1.
Comorbidities tjat are more frequently observed in the patients with CAD with concomitant NAFLD. DM – diabetes mellitus; MS – metabolic syndrome; AH – arterial hypertension; BMI – body mass index.

group 2 (isolated CAD, n=101), which is a significantly lower rate (OR 1.84; 95%, CI 1.080 – 3,134, RR 1,534; p=0.032). Results are presented in Table 2.

Over 2 years of follow-up overall mortality among all patients (n=315) constituted 10.8%. For groups mortality distribution was as follows: group 1 – 13.1%, group 2 – 4.95% (p=0.028), while mortality for cardiovascular reasons in patinets with NAFLD was 8.8% vs. 3.9% (p=0.12), therefore, concomitant NAFLD significantly worsens long-term prognosis. Kaplan-Meier cumulative survival curves in the compared groups are presented on Fig. 2.

There were no statistically significant differences between groups in the occurrence of such end-points as stroke (OR 1.42; 95%, CI 0.2 – 10.01, RR 1.416; p=0.761) and recurrent AMI (OR 2.23; 95% CI 0.767 – 6.441; RR 2.124; p=0.221) (Fig. 3).

Over all period of follow-up patients with CAD+NAFLD showed statistically 3-fold significant faster CHF progression as per hemodynamic indices worsening according to EchoCG repeated examination compared to patients without concomitant NAFLD. Worsening indices in group 1 constituted 11.6% vs. 3.96% (OR 3.35; 95%, CI 1.186 – 9.447; RR 3.068; p=0.023). CHF progression in the patients with CAD+NAFLD may be due to co-existing MS or DM, which promotes further atherosclerosis progression, as well as kidneys damage and dysfunction. According to Giovanni T., Lorenzo B., et al., NAFLD is to a serious extent associated with CVR

Table 2.
AF paroxysm relative risk in the group of CAD+NAFLD vs. CAD group after CABG surgery.

	OR	95% CI		RR	p
Perioperative mortality	-	-	-	-	-
Paroxysmal AF	1.84	1.080	3.134	1.534	0.032

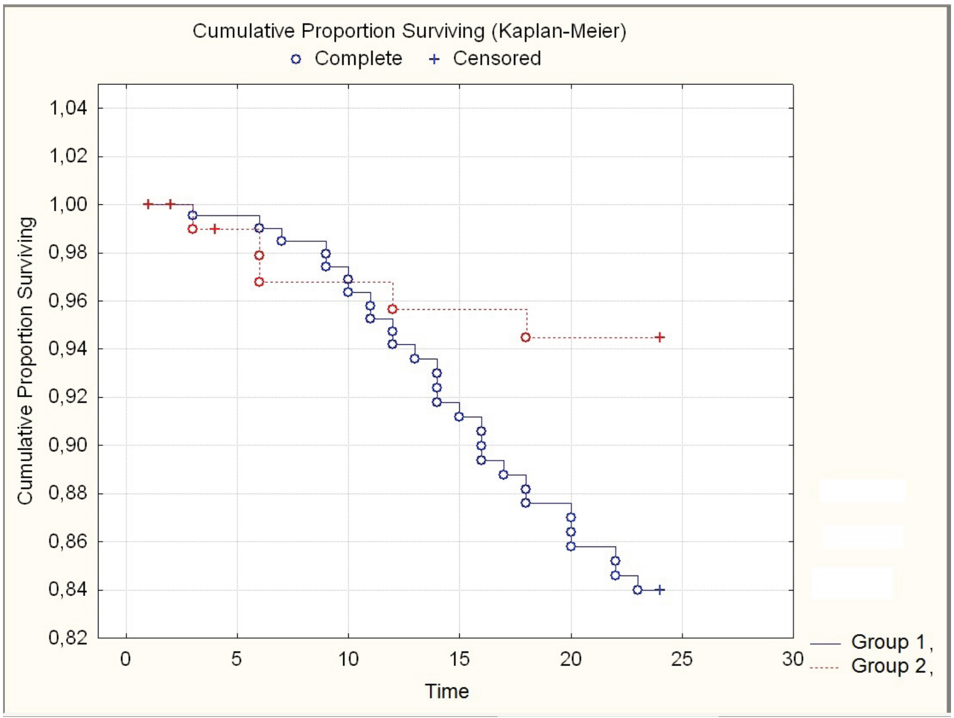

Fig. 2.
Cumulative survival curves in the patients with CAD+NAFLD (group 1) compared to patients ith CAD without NAFLD (Group 2) over 2 years of follow-up

Fig. 3.
Adverse events relative risk in the patients with CAD and NAFLD over 2 years follow-up after CABG

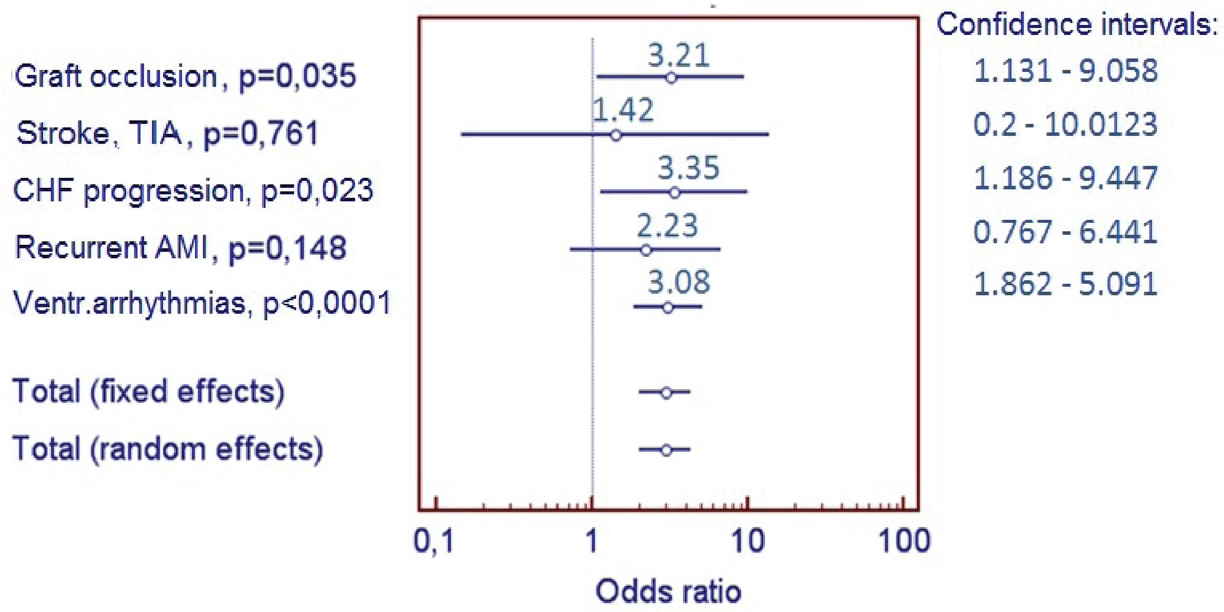

Table 3.
Adverse events relative risk in the patients with CAD+NAFLD vs. Patients with CAD without NAFLD over 2 years of follow-up after CABG

	OR	95% CI	RR	p
Graft occlusion	3.21	1.131-9.058	2.95	0.035
Stroke / TIA	1.42	0.2-10.0123	1.416	0.761
CHF worsening	3.35	1.186-9.447	3.068	0.023
Recurrent AMI	2.23	0.767-6.441	2.124	0.148
Significant ventricular arrhythmias	3.08	1.862-5.091	1.904	<0.0001

increase (OR 3.208; 95% CI 1.4 – 2.1, p<0.001) [6], which is quite consistent with our data. Namely, in such patients we observed significantly more often grafts occlusion after CABG according to contrast coronary MSCT data (OR 3.21, CI 1.31 – 9.058, RR – 2.95, p=0.035); CHF worsening (OR – 3.35, CI 1.186 – 9.447, RR – 3.068, p=0.023), clinically significant ventricular arrhythmias (frequent and paired ventricular extrasystoles, ventricular tachycardia paroxysms (OR 3.08, CI 1.862 – 5.091, RR 1.904, p<0.0001) (Table 3). Therefore, concomitant NAFLD in the patients with CAD is a significant risk factor, which worsens prognosis in the patients after surgeon revascularization.

Conclusions

1. Concomitant NAFLD worsens CAD flow.
2. Concomitant NAFLD in CAD patients is an adverse prognosis marker, as in these patients grafts occlusion, CHF progression and advanced ventricular arrhythmias were significantly more often observed.
3. Risk of AF as CABG surgery complication in the patients with concomitant NAFLD was significantly higher (1.5-fold) compared to patients without NAFLD.
4. Patients with CAD combined with NAFLD have significantly higher mortality rate over two years after CABG compared to those without NAFLD.

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