exclusion of patients because of missing DTB or the time to presentation data could potentially have affected our results.

Our results were also limited to in-hospital outcomes, but benefits of reduced DTB may emerge later, with a reduction in heart failure and a later mortality.

In conclusion, our study found no correlation between short DTB or time to presentation and in-hospital mortality. Further investigation is needed to prove that short DTB does not have an impact on mortality in Japanese STEMI patients.

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Genetic influence in liver steatosis prevalence and proatherothrombotic/inflammatory profile in familial combined hyperlipoproteinemia

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Familial combined hyperlipidemia (FCHL) is the most common atherogenic disorder of lipid metabolism representing the main risk factor in 10–20% of premature myocardial infarction survivors [1]. FCHL is characterized by an increased production of very low density lipoproteins (VLDL)/apolipoprotein B in the liver and impaired catabolism of remnants driving a pro-atherothrombotic lipid profile [2,3]. The genetic defect(s) and detailed pathophysiology are still unknown and the complex polypathogenetic mechanism is reflected by the difficulty to reach a specific genetic trait, clinically available for diagnosis, in FCHL [4] and by a significant overlap with obesity and the metabolic syndrome (MS) [5].

It has been previously demonstrated that hepatic fat accumulation is a common condition in FCHL [6], showing that VLDL production depends on the amount of fat accumulated in the liver [7] with a clinical prevalence of non-alcoholic fatty liver disease (NAFLD) between 49% and 76% in individuals with FCHL [6,8]. NAFLD is a liver disease ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis and cirrhosis [9]. Ample evidence indicates that NAFLD, especially in its necroinflammatory form (NASH), is a source of proatherogenic molecules favoring the progression of cardiovascular disease (CVD), and several genes involved in the pathogenesis or in the protective response to atherothrombosis, have been found to be differentially expressed in patients with NAFLD [9]. Among these, the lectin-like oxidized LDL receptor 1 (LOX-1) transiently removes oxidized LDL from the blood, resulting in complete prevention of atherosclerotic progression, despite the persistence of severe dyslipidemia [10]. In NASH, the LOX-1 polymorphism is associated with liver disease severity, and may predispose to CVD through modulation of adipokine balance [11].

The aim of the present study was to evaluate the distribution of inflammatory and pro-atherothrombotic markers in patients with FCHL according to the presence of liver steatosis and specific genetic traits.

The present was an observational, longitudinal, single-time evaluation study of patients with FCHL with or without NAFLD diagnosed on ultrasonography. This non-invasive method is now proven to safely satisfy the recognition of liver steatosis in the clinical evaluation of patients with metabolic disturbances and increased cardiovascular risk avoiding initially invasive techniques such as liver biopsy [9].

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FCHL was diagnosed according to previously reported criteria [5]. Exclusion criteria were secondary causes of steatosis, including alcohol abuse (≥30 g alcohol daily for men and ≥20 g for women), other forms of liver disease, and use in the previous month of anti-hypertensive, anti-thrombotic, lipid-lowering, anti-inflammatory, except for acetaminophen, and immunosuppressant/immunomodulant drugs.

We evaluated 122 clinically diagnosed FCHL patients out of 226 untreated subjects first-time diagnosed with FCHL. Sixty-two of them had mild or severe liver steatosis and 60 patients did not have liver steatosis. A control group of 60 matched healthy subjects was also recruited (Table 1).

Patients and controls were compared for complete lipid profile, transaminases, homeostasis model assessment (HOMA)-index, as well as for circulating levels of soluble CD40 ligand (sCD40L), Endogenous Thrombin Potential (ETP), tumor-necrosis factor (TNF)-α, interleukin (IL)-6 and -10, adiponectin, leptin, and high sensitivity C-reactive protein (hs-CRP) as previously described [12–14]. Furthermore, each patient was genotyped for Adiponectin 45TT and 256 GT/TT, (Genbank Accession no. NM_004797), IL10 10-1082A, (X73536), LOX-1 IVS4-14 A/G, (NM_002543) (Loxin Test®Technogenetics, Sesto San Giovanni, Italy), and nitric oxide synthase (NOS) G894T polymorphism, (D26607), using DNA extraction techniques, specific primers and polymerase chain reaction as previously described on a ABI-PRISM 7000 detection system (Applied Biosystems, Foster City, CA) [15–17].

Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. The Mann–Whitney *U*-test and the Wilcoxon test were used for comparisons between and within groups. A multiple logistic regression analysis was employed to evaluate the putative relations among the percent range transformed measurable studied variables (5% difference steps) and nonparametric data such as genetic traits and/or the presence of liver steatosis. Furthermore a formal test for interaction was employed to determine the putative relation for each single variable and final validation of data was assessed by a resampling technique (exact tests in SPSS 2003 module) and discrimination analysis by the Hosmer–Lemeshow method as described in detail elsewhere [18]. Finally, Receiver Operating Characteristic curve (ROC curve) and training set Area Under Curve (AUC) were evaluated by parametric method using a maximum likelihood estimator to fit a smooth curve to the data points by a specific computed method (SPSS 2003 module). Each cluster of polymorphisms has been categorized with a different numeric value for this analysis. The Hanley–McNeil method and the z test were employed to determine the relations and differences between

Table 1
Baseline characteristics of patients with FCHL with and without NAFLD, and controls.

	Whole FCHL cohort (n = 122)	P value (FCHL vs controls)	Controls (n = 60)	P value (controls vs NAFLD +)	NAFLD + (n = 62)	P value (NAFLD + vs NAFLD −)	NAFLD − (n = 60)	P value (NAFLD − vs controls)
Age (yrs)	56.6 ± 6.6	0.085	60.1 ± 7.5	0.114	55.6 ± 6.1	0.139	57.6 ± 6.9	0.111
Male gender — no. (%)	78 (64)	0.042	31 (52)	0.129	41 (66)	0.089	37 (62)	0.118
Smokers >5 cig/day	30%	0.106	32%	0.103	31%	0.156	29%	0.126
Physical activity								
Low	23%	0.083	26%	0.091	23%	0.135	22%	0.085
Moderate	76%	0.127	74%	0.279	74%	0.116	76%	0.129
Intense	1%	0.001		0.001	3%	0.099	2%	0.001
BMI (kg/m^2)	25.4 ± 0.7	0.091	24.8 ± 0.3	0.094	25.3 ± 0.5	0.114	25.4 ± 0.6	0.091
WC (cm)								
Male	96.4 ± 5.8	0.088	95.8 ± 5.6	0.090	96.3 ± 5.9	0.113	96.5 ± 5.4	0.089
Female	82.1 ± 4.8	0.097	81.6 ± 4.4	0.096	82.3 ± 4.7	0.091	81.7 ± 4.8	0.095
SBP (mm Hg)	125.2 ± 8.4	0.103	124.7 ± 9.1	0.081	125.6 ± 8.2	0.096	124.8 ± 8.3	0.099
DBP (mm Hg)	77.8 ± 7.9	0.094	77.3 ± 8.5	0.095	78.1 ± 7.1	0.090	77.5 ± 8.2	0.119
Lipid profile								
Total cholesterol (mmol/L)	6.62 ± 0.25	0.001	4.8 ± 0.16	0.001	6.61 ± 0.25	0.111	6.63 ± 0.24	0.001
HDL-cholesterol (mmol/L)	1.27 ± 0.09	0.059	1.38 ± 0.09	0.055	1.26 ± 0.12	0.081	1.27 ± 0.09	0.058
Triglycerides (mmol/L)	1.73 ± 0.14	0.095	1.20 ± 0.13	0.091	1.77 ± 0.14	0.099	1.69 ± 0.12	0.099
LDL-cholesterol (mmol/L)	4.55 ± 0.22	0.001	2.85 ± 0.13	0.001	4.53 ± 0.21	0.102	4.57 ± 0.22	0.001
Apo-B (g/L)	15.2 ± 0.95	0.002	9.96 ± 0.72	0.002	15.2 ± 0.97	0.138	15.1 ± 0.94	0.002
Apo-A (g/L)	9.7 ± 0.93	0.077	10.7 ± 0.68	0.078	9.7 ± 0.93	0.127	9.7 ± 0.91	0.075
Apo-B/A	1.55 ± 0.14	0.004	0.93 ± 0.09	0.043	1.55 ± 0.15	0.087	1.54 ± 0.13	0.043
Ox-LDL (IU/L)	101.2 ± 10.4	0.005	59.4 ± 7.6	0.003	109.6 ± 9.3	0.036	92.7 ± 10.8	0.009
History of prev hyperTC	61%	–	–	–	59%	0.076	62%	–
History of prev hyperTG	39%	–	–	–	41%	0.072	38%	–
History of low HDL-C	39%	–	–	–	55%	0.031	31%	–
Glucose (mmol/L)	5.16 ± 0.20	0.097	5.1 ± 0.15	0.092	5.18 ± 0.20	0.103	5.13 ± 0.18	0.099
Insulin (μU/mL)	5.78 ± 1.11	0.069	5.04 ± 1.12	0.061	5.99 ± 1.07	0.079	5.61 ± 1.13	0.078
HOMA-IR index	1.12 ± 0.11	0.078	1.06 ± 0.07	0.077	1.12 ± 0.11	0.088	1.11 ± 0.09	0.080
Adiponectin (μg/mL)	9135.5 ± 146.9	0.001	13964.5 ± 147.4	0.001	7229.4 ± 112.6	0.009	11041.6 ± 139.7	0.058
Leptin (ng/mL)	12179.9 ± 325.2	0.090	11098.4 ± 286.9	0.086	12250.5 ± 326.4	0.105	12109.4 ± 318.8	0.094
Hs-CRP (mg/mL)	1.34 ± 0.13	0.061	0.97 ± 0.11	0.059	1.38 ± 0.14	0.083	1.31 ± 0.12	0.065
TNF-α (pg/mL)	3.74 ± 1.14	0.089	2.94 ± 0.93	0.071	3.94 ± 1.14	0.076	3.55 ± 1.12	0.095
IL-6 (pg/mL)	3.41 ± 0.79	0.090	2.87 ± 0.57	0.095	3.37 ± 0.85	0.091	3.46 ± 0.66	0.086
IL-10 (pg/mL)	1.45 ± 0.24	0.039	2.97 ± 0.26	0.001	0.96 ± 0.21	0.001	1.95 ± 0.22	0.063
ALT (IU/L)	35.6 ± 4.1	0.068	24.7 ± 2.8	0.042	40.4 ± 4.2	0.061	30.1 ± 3.5	0.096
γ-GT (IU/L)	44.1 ± 10.1	0.067	32.9 ± 5.5	0.0511	49.3 ± 10.4	0.055	38.9 ± 9.2	0.091
sCD40L (pg/mL)	546.1 ± 29.5	0.002	129.4 ± 32.5	0.001	675.8 ± 31.6	0.036	416.3 ± 23.2	0.00496
ETP (Δ% from reference)	41.4 ± 3.8	0.001	3.1 ± 0.2	0.001	48.4 ± 3.9	0.039	34.6 ± 3.6	0.001
Fatty Liver Index (FLI)	41 ± 8	0.056	27 ± 6	0.0506	45 ± 8§	0.660	37 ± 9	0.061

Abbreviations: ALT: Alanine Transaminase; AST: Aspartate Transaminase; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein.
SI Conversions: To convert total and HDL cholesterol to mg/dL, multiply by 38.6; to convert triglycerides to mg/dL, multiply by 88.6; to convert glucose to mg/dL multiply by 18.0.