

**Retraction Notice**

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## Fatty liver disease might increase the risk of abdominal operation in patients with fatty liver and the prevalence of cancer in first-degree relatives

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### ABSTRACT

**Background/Aims:** We investigated the risk of abdominal operation in patients with fatty liver and the risk of any cancer in first-degree relatives of patients with fatty liver.

**Materials and Methods:** We evaluated 105 patients with nonalcoholic fatty liver disease (NAFLD), 121 patients with biopsy-proven hepatitis C (61 patients with fatty liver and 60 patients without fatty liver), 50 patients with inflammatory bowel disease (IBD), and 109 patients with dyspepsia.

**Results:** There was no difference in sex, mean age, and marital status among the groups except that patients with IBD were younger than the others ( $p < 0.001$ ). The frequency of cancer among family members was 18% in IBD, 9% in dyspepsia, 28% in hepatitis C with steatosis, 21.5% in hepatitis C without steatosis, and 27% in NAFLD ( $p = 0.006$ ). Then, we divided the study group into two groups as follows: group 1: (IBD + dyspepsia + hepatitis C without steatosis) and group 2: (hepatitis C with steatosis + NAFLD). We found that the frequency of cancer was 16% in group 1 versus 24.4% in group 2 ( $p = 0.037$ ). We also investigated the risk of abdominal operation in patients with fatty liver. The results were as follows: 33% in group without fatty liver versus 43% in group with fatty liver ( $p = 0.043$ ).

**Conclusion:** Understanding the underlying causes of fatty liver forms might decrease the cancer frequency in the population and number of operations in patients with fatty liver.

**Keywords:** Abdominal operation, cancer, dyspepsia, fatty liver, hepatitis C, nonalcoholic

### INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is one of the most prevalent forms of chronic liver diseases in gastroenterology and hepatology practices (1,2). Contributing factors to this include the increasingly sedentary lifestyle of the population, besides the increased consumption of a high-fat (HF) diet and high-fructose corn syrup (HFCS) (3-5). It is now accepted that in the setting of excessive central adiposity, insulin resistance is the major underlying cause of fat accumulation in the liver (6-10). Insulin resistance and the metabolic syndrome are growing threats to the health of people in developed nations (1,2). NAFLD has the potential to progress to cirrhosis, hepatocellular carcinoma (HCC), end-stage

liver disease, and liver transplantation (11-16). However, one of the most important and unresolved problems is the pathogenesis and underlying mechanisms in the development of NAFLD, despite the growing body of literature (17-22). In this study, we investigated the risk of abdominal operation in patients with fatty liver. Additionally, the risk of cancer in the first-degree relatives of patients with fatty liver was evaluated.

### MATERIALS AND METHODS

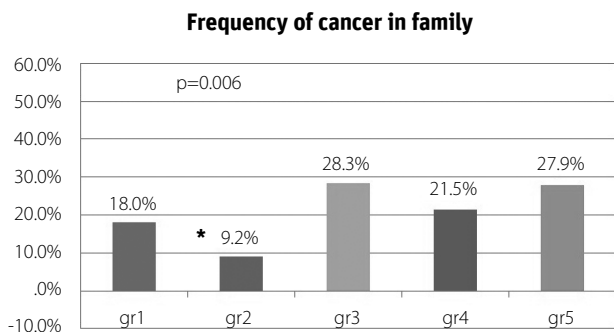
A randomized prospective study was performed at the Department of Gastroenterology, Bezmialem Vakıf University, İstanbul, Turkey. The local ethic committee approved this study.

This study was presented by Dr. Hakan Şentürk as a poster at the 63<sup>rd</sup> Annual Meeting of the American Association for the Study of Liver Disease (AASLD), 9-13 November 2012, Boston, USA.

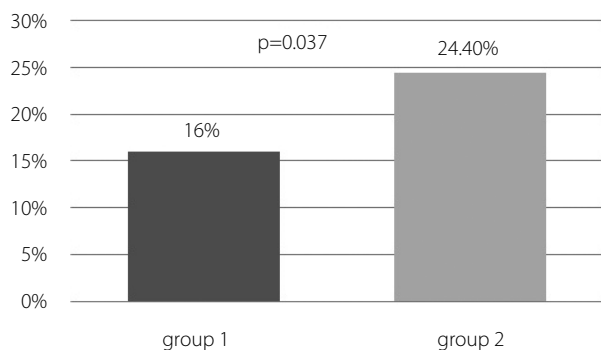
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**Figure 1.** The frequency of cancer in family members was 18% in IBD (gr1), 9% in dyspepsia (gr2), 28% in hepatitis C with steatosis (gr3), 21.5% in hepatitis C without steatosis (gr4), and 27.9% in NAFLD (gr5) (p=0.006 among the groups). There was no difference among the groups in cancer frequency after the exclusion of patients with dyspepsia (p>0.05).



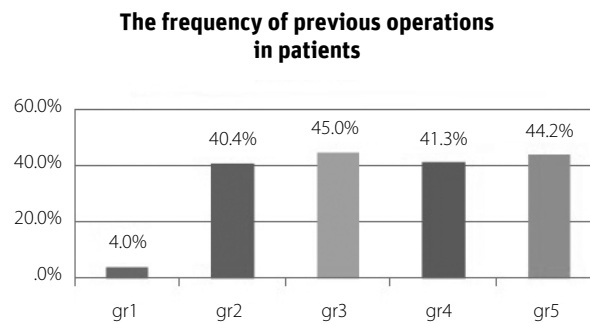
**Figure 2.** After dividing the study group into two groups as group 1: IBD + dyspepsia + hepatitis C without steatosis and group 2: hepatitis C with steatosis + NAFLD, we performed the analysis: 16% in group 1 without fatty liver vs. 24.4% in group 2 with fatty liver (p=0.037).

Alcohol history was excluded from each patient by self-report, and an alcohol abuse history was taken from family members for each patient. Any drug history or history of chronic hepatitis, hypertension, and diabetes were all questioned. Ultrasonographic evaluation of the hepatobiliary system was performed. A fatty liver was diagnosed by increased echogenicity or increased liver-kidney contrast. Serum serology of HBsAg (hepatitis B surface antigen), anti-HBs (anti-hepatitis B surface), anti-HBc-total (anti-hepatitis B core-total), and anti-HCV (anti-hepatitis C virus) was measured. If necessary, liver biopsies were processed and read by a single pathologist. NAFLD was diagnosed by experienced pathologists according to standard criteria (23-25).

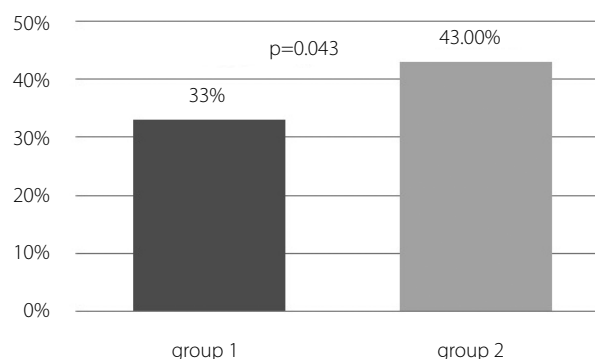
We first performed a power analysis/sample size determination (a single-sample z-test) for the proportion. We evaluated 105 patients with NAFLD, 121 patients with hepatitis C (61 with hepatic steatosis, and 60 without steatosis), 50 patients with inflammatory bowel disease (IBD), and 109 patients with dyspepsia.

**Statistical analysis**

The data were presented as mean±SD and were analyzed by SPSS 13 (SPSS Inc, Chicago, IL, USA). Features of groups were



**Figure 3.** The frequency of operation was 4% in patients with IBD (after the exclusion of intestinal surgeries due to IBD), 40% in dyspepsia, 45% in hepatitis C with steatosis, 41% in hepatitis C without steatosis, and 44% in NAFLD, respectively (p=0.001 among the groups). There was no difference among the groups in the operation frequency after the exclusion of patients with IBD (p>0.05).



**Figure 4.** The frequency of operation in patients with fatty liver was 33% in group 1 without fatty liver vs. 43% in group 2 with fatty liver (p=0.043). Group 1: IBD + dyspepsia + hep C without fatty liver. Group 2: hep C with steatosis + NAFLD.

compared with each other by t-test and chi-square test. Probability (p) values <0.05 were considered statistically significant.

**RESULTS**

There was no difference in sex, mean age, and marital status among the groups except that patients with IBD were younger than others (p<0.001). The frequency of cancer in their first-degree relatives was 18% in IBD, 9% in dyspepsia, 28% in hepatitis C with steatosis, 21.5% in hepatitis C without steatosis, and 27% in NAFLD (p=0.006 among the groups), as shown in Figure 1. After the exclusion of patients with dyspepsia, there was no significant difference among the groups. Then, we divided the study group into two groups-group 1: IBD + dyspepsia + hepatitis C without steatosis; and group 2: hepatitis C with fatty liver steatosis + NAFLD-and performed the analysis. We found that the frequency of cancer was 16% in group 1 without fatty liver versus 24.4% in group 2 with fatty liver (p=0.037), as shown in Figure 2.

In the second part of the study, we investigated the frequency of operation in patients with fatty liver. We found that the frequency of operation in patients with fatty liver was 4% in IBD (after

the exclusion of intestinal surgeries due to IBD), 40% in dyspepsia, 45% in hepatitis C with steatosis, 41% in hepatitis C without steatosis, and 44% in NAFLD ( $p=0.001$  among the groups), as shown in Figure 3. On further analysis, the prevalence of operations was 33% in group 1 without fatty liver versus 43% in group 2 with fatty liver ( $p=0.043$ ), as shown in Figure 4.

## DISCUSSION

In this study, we showed an increase in both the frequency of operations in patients with fatty liver and the frequency of cancer in their first-degree relatives, independent of the underlying chronic disease. All of these results were obtained independently of sex, mean age, and marital status of the patients. We showed that the frequency of cancer among the family members was 9% in dyspepsia, 21.5% in hepatitis C without steatosis, 28% in hepatitis C with steatosis, and 27% in NAFLD, respectively. These results indicated that fat accumulation in the liver might increase the cancer rate among family members. We consider that obesity-induced fatty liver has a more detrimental effect on the body system than hepatitis C-induced fatty liver. Then, we divided the study group into two big groups by the occurrence of fat to see whether there were any changes in the statistical results: group 1: (IBD + dyspepsia + hepatitis C without steatosis) and group 2: (hepatitis C with steatosis + NAFLD). As expected, although the frequency of cancer was 16% in group means none fat group, the frequency of cancer reached 24.4% in the fatty liver group, with statistical significance ( $p=0.037$ ).

In this study, we also investigated the risk of abdominal operation in patients with fatty liver. The abdominal operation rate was 33% in patients without fatty liver. On the other hand, 43% of patients with fatty liver underwent abdominal operation previously. These frequencies were statistically meaningful ( $p=0.043$ ).

A growing body of literature has indicated that there is an association between obesity, type 2 diabetes mellitus, and particular cancer types, such as enhanced risk of colorectal, esophageal, and kidney cancer, by large epidemiological studies (12-15). This risk was maintained, even after adjusting for factors, such as BMI, family history, physical activity, smoking, red meat consumption, hormone, and aspirin use. The cause of these findings was not investigated in this study. However, shared mechanisms in the development of fatty liver disease and cancer might be a reason of the increased frequency of cancer rates. Some genes, ligands, and various factor receptors (insulin, IGF1 axis, ectopic E synthesis, adipokines, PTEN, PI3K, mTOR, MAPK, HIF-1 $\alpha$ , COX-2, MIF), might increase the risk of cancer, which might be dealing with the pathogenesis of fatty liver.

On the other hand, an impaired immune system is one of the underlying mechanisms in the development of fatty liver (1-4,7,18,19). Patients with fatty liver have chronic low-grade in-

flammation. Thus, increased systemic body inflammation and its consequences might lead to increased frequency of operations in patients with fatty liver.

In conclusion, independent of the underlying chronic disease, the occurrence of fat in the liver increases both the frequency of operations in patients with fatty liver and the frequency of cancer in their first-degree relatives. These findings indicate that we should carefully focus on the prevention and therapy of fatty liver. Understanding the underlying causes of fatty liver forms the basis for rational preventive and treatment strategies. These attempts might decrease the cancer frequency in the population and number of operations in patients with fatty liver.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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