Relationship between diverticulosis and nonalcoholic fatty liver disease in elderly patients

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Abstract

Objective: To compare clinical and laboratory features of elderly patients with and without diverticulosis and assess factors related to hepatosteatosis.

Method: This retrospective case–control study analysed the clinical and laboratory data, colonoscopy and abdominal ultrasonography records of patients >65 years who underwent colonoscopies. Subjects were categorized according to the presence and absence of colonic diverticulosis. Univariate/multivariate logistic regression analyses were performed to evaluate the independent predictive factors of hepatosteatosis.

Results: A total of 355 patients were enrolled in the study: 169 had colonic diverticulosis; and 186 without colonic diverticulosis formed the control group. Age, sex and chronic disorders associated with the metabolic syndrome did not differ between the diverticulosis and control groups. The rate of hepatosteatosis was lower in patients with diverticulosis compared with the control group (27% versus 42%, respectively). Diabetes mellitus, hyperlipidaemia and hepatosteatosis were more common among patients aged <75 years. In the multivariate logistic regression analysis, diverticulosis remained an independent predictor of hepatosteatosis (odds ratio 0.529; 95% confidence interval 0.323, 0.866). Other independent predictive factors in the multivariate analysis were triglyceride and albumin.

Conclusion: Diverticulosis in the elderly was found to be a negative predictor of hepatosteatosis. Higher values of albumin and triglyceride in conjunction with the absence of diverticulosis may be suggestive of nonalcoholic fatty liver disease in the elderly.

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease, affecting 20% to 30% of adults in developed countries and up to 80% of obese people.[1,2] NAFLD is characterized by hepatocellular fat deposition accounting for more than 5% of the liver's weight and includes simple steatosis and nonalcoholic steatohepatitis (NASH), which is associated with or precedes metabolic syndrome.[2] Epidemiological studies have shown an 'inverted U-shape' distribution in the incidence of NAFLD, with the incidence decreasing after the 6th decade in men and the 7th decade in women; however, more severe histological changes occur with advanced age.[3] Tissue inflammation and oxidative stress resulting in NASH and cirrhosis are more pronounced with aging.[3]

Diverticulosis is also a common condition after a person reaches their 50s.[4] It is rare below the age of 40 years and the prevalence increases with age.[5] One-third of the population will have diverticulosis by the age of 60, and two-thirds will have it by the age of 85 in Western countries.[5,6] Diverticulosis is more common in Western countries than in Africa and Asia.[7] Several risk factors for diverticulosis have been identified, such as older age, constipation, a high intake of red meat, a low-fibre diet, and a low level of physical activity.[8]

Another important and increasingly recognized issue in the elderly population is malnutrition, including undernutrition, overnutrition and specific nutrient deficiencies.[9] The prevalence of malnutrition differs among different geriatric groups.

For example, although malnutrition is found in 23–60% of older hospitalized patients, the reported prevalence of malnutrition in community dwelling older adults is relatively low (5–10%).[10,11] Among community dwelling older adults, the prevalence of malnutrition is two-fold higher in those aged 75–80 years compared with those aged 65–74 years.[12] Several nutritional tools have been used for the nutritional screening of older subjects.[13] In addition to these tools, a serum protein, albumin, has been accepted as a good marker of nutritional status in elderly patients.[14]

A Western-type diet including a low fibre intake is associated with obesity and metabolic syndrome.[15] As stated earlier, colonic diverticulosis is also related to a low fibre intake.[8] Nutritional habits and the aging process seem to influence the occurrence and severity of both diverticulosis and NAFLD.[3,16] However, it has not been established whether diverticulosis is associated with NAFLD, which is closely associated with the metabolic syndrome in the elderly.[17] The current study aimed to investigate the presence of hepatosteatosis (HS) in patients with diverticulosis and compare them with sex- and age-matched control subjects without diverticulosis. Clinical features and laboratory factors associated with HS were also examined.

Patients and methods

Study population

This retrospective case–control study enrolled consecutive patients aged >65 years

who underwent a colonoscopic examination at the Department of Internal Medicine, Division of Gastroenterology and Hepatology, Firat University School of Medicine, Elazig, Turkey between January 2011 and April 2016. Patients with colonic diverticulosis who had a laboratory assessment and ultrasonography were recruited to the study; and sex- and age-matched subjects with normal colonoscopic features (i.e. without diverticulosis) were recruited as a control group. Ethical approval for the study was obtained from the Institutional Review Board of Firat University Medicine Faculty (no. 31.05.2016/10/08). Informed patient consent was not required because of the retrospective nature of this study.

Data collection

Demographic data, clinical characteristics and chronic disorders, including diabetes mellitus (DM), hypertension (HT), hyperlipidaemia (HL) and coronary arterial disease (CAD), were recorded. Complete blood count, fasting glucose, liver function tests, bilirubin, albumin, uric acid, lipid panel and radiology reports were obtained from the hospital records and the hospital database.

Ultrasonographic assessment of hepatosteatosis

An ultrasonographic assessment was performed by one radiologist who was experienced in abdominal ultrasound using a 3.5-MHz convex probe on an Aplio XG ultrasound machine (Toshiba Medical Systems, Ottawara, Japan). HS was graded according to the severity of steatosis: (i) normal (grade 0); (ii) liver attenuation slightly less than the spleen (grade 1); (iii) more pronounced difference between liver and spleen and intrahepatic vessels not seen or at a slightly higher attenuation than the liver (grade 2); and (iv) markedly reduced liver attenuation with a sharp contrast between the liver and intrahepatic vessels (grade 3).[18] Patients were diagnosed as NAFLD after excluding all other liver diseases including cirrhosis, any cause of chronic hepatitis and alcoholic steatohepatitis based on data obtained from the hospital records. Exclusion criteria included the following: (i) lack of laboratory data; (ii) lack of an ultrasonographic assessment; (iii) those with disorders related to HS such as coeliac disease and jejunoileal bypass; (iv) patients who used medications such as amiodarone, methotrexate, tetracycline, tamoxifen and antiretroviral drugs; (v) patients with active malignancy, hypothyroidism, hyperthyroidism and rheumatological and inflammatory disorders; (vi) patients receiving niacin, a high-density lipoprotein cholesterol (HDL-C)-lowering medication.

Statistical analyses

All statistical analyses were performed using the SPSS® statistical package, version 22.0 (SPSS Inc., Amrok, NY, USA) for Windows®. The Shapiro–Wilk test was used to evaluate the distribution of the variables. Categorical variables are presented as frequencies and percentages. Normally distributed continuous variables are expressed as mean $\pm$ SD, whereas skewed distributed continuous variables are expressed as median $\pm$ SE. In the analysis of statistical significance, an independent-sample Student's t-test was implemented for normally distributed variables, and the Mann–Whitney U-test was performed for variables that were not normally distributed. The χ^2-test, where appropriate, was used to compare the proportions in different groups. For the multivariate analysis, the variables that had P-values < 0.1 on univariate logistic regression analysis were further evaluated in multivariate logistic regression

analysis to determine independent predictors of HS. A *P*-value < 0.05 was considered statistically significant unless otherwise stated.

Results

A total of 2612 patients aged >65 years underwent a colonoscopic examination between January 2011 and April 2016 and diverticulosis was detected in 410 (15.7%). A total of 169 patients aged >65 years with diverticulosis and 186 patients aged >65 years with normal colonoscopic findings were recruited into the study. The mean ± SD age of the entire study population was 74.8 ± 6.4 years and 211 (59.4%) were male. The demographic, clinical and laboratory characteristics of the two groups of participants are presented in Table 1. There were no significant differences between the two groups in terms of age, sex distribution and the presence of chronic disorders associated with the metabolic syndrome such as DM, HT, HL and CAD.

Hepatosteatosis was more common among control subjects without diverticulosis than patients with diverticulosis (42% versus 27%, respectively; *P* = 0.004) (Table 1). The laboratory data for patients with and without diverticulosis are shown in Table 1. The erythrocyte sedimentation rate was significantly higher in the diverticulosis group compared with the control group without diverticulosis (*P* = 0.049). The median alkaline phosphatase value was significantly higher in the control group than in the diverticulosis group (*P* = 0.001). In contrast, the median uric acid level was significantly higher in the diverticulosis group than in the control group (*P* = 0.021).

The study population was divided into groups of those <75 (*n* = 207) and those ≥75 years (*n* = 148) and several analyses were undertaken. Diabetes mellitus and hyperlipidaemia were significantly more common among those <75 years compared with those ≥75 years (*P* = 0.021 and *P* = 0.002, respectively). Hepatosteatosis was also significantly more prevalent among those <75 years (43%) when compared with those ≥75 years (24%) (*P* < 0.001). Haemoglobin, alanine aminotransferase, albumin, triglyceride and HDL-C values were significantly higher in those <75 years when compared with those ≥75 years (*P* < 0.05 for all comparisons). However, the erythrocyte sedimentation rate and C-reactive protein values of those ≥75 years were significantly higher than those <75 years (*P* < 0.05 for all comparisons). Although statistical significance was not reached, diverticulosis was found to be more common among those ≥75 years than in those <75 years (53% versus 43%, respectively).

Hepatosteatosis was detected in 124 patients (35%) in the entire study population. Although sex did not differ between groups according to the presence or absence of HS, those patients with normal ultrasonography were significantly older than the those with HS (75.8 ± 6.4 versus 73.0 ± 6.1, respectively; *P* < 0.001). Univariate analysis for the identification of the presence of hepatosteatosis demonstrated that age, DM, HT, the presence of diverticulosis, haemoglobin, platelet count, alanine aminotransferase, albumin, serum triglyceride, HDL-C and erythrocyte sedimentation rate were statistically significant independent predictive factors (Table 2). Variables that were statistically significant in the univariate logistic regression model were further subjected to a multivariate logistic regression analysis and serum triglyceride, albumin and the presence of diverticulosis remained statistically significant independent predictors for the presence of hepatosteatosis (Table 3).

Discussion

Extensive epidemiological data exists regarding diverticulosis, but little research

Table 1. Demographic, clinical and laboratory characteristics of patients with and without diverticulosis who were enrolled in this study of the relationship between diverticulosis and nonalcoholic fatty liver disease.

Characteristic	Diverticulosis group $n = 169$	Control group $n = 186$	Statistical significance[a]
Age, years*	75.4 ± 6.3	74.2 ± 6.4	NS
Sex, male	102 (60)	109 (59)	NS
Associated disorders,			
Diabetes mellitus	46 (27)	59 (32)	NS
Hypertension	100 (59)	111 (60)	NS
Hyperlipidaemia	40 (24)	61 (33)	NS
Coronary artery disease	64 (38)	67 (36)	NS
Diverticular localization			
Left side	90 (53)	–	
Right side	16 (9)	–	
Bilateral	63 (37)	–	
Hepatosteatosis,	46 (27)	78 (42)	$P = 0.004$
Grade I	40 (24)	59 (32)	
Grade II	6 (4)	19 (10)	
WBC, $\times 10^3/\mu l$	7120 ± 173	7085 ± 141	NS
Haemoglobin, g/dl*	12.9 ± 2.0	12.9 ± 2.1	NS
Platelet count, $\times 10^3/\mu l$	252 ± 7	247 ± 6	NS
Fasting glucose, mg/dl	100 ± 3	104 ± 3	NS
ALT, U/l	17 ± 1	18 ± 1	NS
AST, U/l	22 ± 1	21 ± 1	NS
GGT, U/l	20 ± 2	18 ± 2	NS
ALP, U/l	67 ± 2	78 ± 2	$P = 0.001$
Bilirubin, total, mg/dl	0.60 ± 0.03	0.60 ± 0.02	NS
Bilirubin, direct, mg/dl	0.20 ± 0.01	0.20 ± 0.01	NS
Uric acid, mg/dl	6.0 ± 0.1	5.5 ± 0.1	$P = 0.021$
Albumin, g/dl*	4.02 ± 0.53	4.13 ± 0.42	$P = 0.035$
Triglyceride, mg/dl	125 ± 5	121 ± 4	NS
LDL-C, mg/dl	116 ± 3	117 ± 3	NS
HDL-C, mg/dl	46 ± 1	43 ± 1	NS
ESR, mm/h	19 ± 2	17 ± 1	$P = 0.049$
CRP, mg/l	3.3 ± 2.1	3.4 ± 0.4	NS

Data are expressed as mean $\pm$ SD*, n of patients (%) and median $\pm$ SE.
WBC, white blood cell count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NS, no significant between-group difference ($P \geq 0.05$).

has been undertaken on metabolic syndrome-related disorders in individuals with diverticular disease.[19–21] Obesity has been linked to diverticular disease, suggesting that further investigations into the relationship between diverticulosis and NAFLD are required.[21]

The prevalence of colonic diverticulosis was estimated to be 15.7% among individuals over 65 years in the current study. A study from Saudi Arabia found that the prevalence of diverticulosis was 7.4%, and 61% of them were male.[22] Recent data from Israel showed a 17.4% prevalence of

Table 2. Univariate logistic regression analyses for variables associated with hepatosteatosis in patients with and without diverticulosis who were enrolled in this study of the relationship between diverticulosis and nonalcoholic fatty liver disease.

Variable	Odds ratio	95% confidence interval	Statistical significance
Age	0.928	0.893, 0.964	$P < 0.001$
Sex	1.272	0.817, 1.979	NS
Diabetes mellitus	2.426	1.515, 3.883	$P < 0.001$
Hypertension	1.629	1.033, 2.568	$P = 0.03$
Diverticulosis	0.518	0.331, 0.809	$P = 0.004$
WBC	1.000	1.000, 1.000	NS
Haemoglobin	1.187	1.060, 1.329	$P = 0.003$
Platelet count	0.997	0.994, 1.000	$P = 0.04$
Fasting glucose	1.004	0.999, 1.009	NS
ALT	1.036	1.012, 1.060	$P = 0.003$
AST	1.006	0.981, 1.031	NS
GGT	0.998	0.989, 1.007	NS
ALP	1.002	0.994, 1.011	NS
Albumin	3.231	1.848, 5.649	$P < 0.001$
Triglyceride	1.009	1.005, 1.013	$P < 0.001$
HDL-C	0.982	0.966, 0.998	$P = 0.03$
LDL-C	1.001	0.995, 1.006	NS
ESR	0.980	0.966, 0.994	$P = 0.006$
CRP	0.988	0.970, 1.007	NS

WBC, white blood cell count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NS, not significant ($P \geq 0.1$).

Table 3. Multivariate logistic regression analyses using variables with a *P*-value of <0.1 identified from the univariate regression analysis of variables associated with hepatosteatosis in patients with and without diverticulosis who were enrolled in this study of the relationship between diverticulosis and nonalcoholic fatty liver disease.

Variable	B	Odds ratio	95% confidence interval	Statistical significance
Age	−0.310	0.969	0.926, 1.014	NS
Diabetes mellitus	0.504	1.655	0.955, 2.866	NS
Hypertension	0.305	1.357	0.807, 2.281	NS
Diverticulosis	−0.618	0.529	0.323, 0.866	$P = 0.014$
Haemoglobin	0.027	1.028	0.888, 1.189	NS
Platelet count	−0.002	0.998	0.995, 1.002	NS
ALT	0.100	1.021	0.996, 1.046	NS
Albumin	0.786	2.195	1.122, 4.295	$P = 0.022$
Triglyceride	0.007	1.007	1.002, 1.011	$P = 0.003$
HDL-C	−0.017	0.983	0.964, 1.002	NS
ESR	−0.005	0.995	0.978, 1.012	NS

ALT, alanine aminotransferase; HDL-C, high-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; NS, not significant ($P \geq 0.05$).

diverticulosis with a male predominance (83%).[21] Studies from the Mediterranean area also showed similar rates of diverticulosis.[23,24] East Asian studies demonstrated similar rates of diverticulosis. For example, a study in Taiwan reported a prevalence of diverticulosis of 13.5%;[25] and a recent study from Japan showed a prevalence of 20.3% among a large number of patients who underwent colonoscopic examination.[26] Lower rates of diverticulosis in the Mediterranean area compared with North Europe and the USA, where diverticulosis reaches up to 60% in older subjects, may be related to genetic factors and the Mediterranean diet.[16,27]

Data regarding the burden of NAFLD in elderly people are scarce. A recent meta-analysis on the global epidemiology of NAFLD estimated the prevalence of NAFLD all over the world to be 25%, with the highest prevalence in the Middle East and South America.[2] This meta-analysis also demonstrated that prevalence rates are higher in older subjects, with a 28.90% rate in the 6th decade and 33.99% rate in the 7th decade.[2] NAFLD was present in 35% of the current study population, the mean $\pm$ SD age of which was 74.8 ± 6.4 years. Similar results were seen in the Rotterdam study that NAFLD prevalence was 35.1% among 2811 participants, with a mean $\pm$ SD age of 76.4 ± 6.0 years.[28] According to the subgroups of the Rotterdam study, NAFLD was found in 35.8% of subjects <70 years, in 39.6% of those between 75 and 79 years old, in 32.1% of those between 80 and 84 years old and in 21.1% of subjects >85 years.[28] In accordance with this study,[28] this current study demonstrated a decline in the prevalence of HS among those patients $\geq$75 (24%) compared with patients <75 (43%). Data on NAFLD prevalence in the elderly, which shows an inverted U-shaped curve declining with advanced age, was confirmed in these two studies.[29]

Nonalcoholic fatty liver disease is the hepatic manifestation of metabolic syndrome.[30] The key event in the emergence of metabolic syndrome is insulin resistance.[31] Due to the retrospective nature of the current study, some of the factors necessary for the assessment of metabolic syndrome and insulin resistance, including height, weight, body mass index, waist circumference and serum insulin levels, were lacking. Thus, the current results could not show metabolic alterations that were consistent with the radiological findings. This is a major limitation of the present study. Similarly, a thorough nutritional assessment of the study participants, which can be determined using several indices, questionnaires, anthropometric measurements and a dietary history, was also lacking. Therefore, it was not possible to draw conclusions on the nutritional status of the study participants. However, albumin, which is an accepted indirect indicator of nutritional status in the elderly, was used to evaluate nutritional status in the present study.[14] Moreover, the current study found that albumin was one of the independent predictors of NAFLD.

One of the most notable findings of this current study was that the rate of HS was lower in patients in whom diverticulosis was detected in colonoscopic examinations (27%) than in those without diverticulosis (42%). Moreover, the absence of diverticulosis was one of the independent predictors of NAFLD in a multivariate analysis. These findings suggest that diverticulosis might be a protective factor for hepatosteatosis, but the underlying mechanisms remain unclear. It may be an indirect sign of undernutrition in the elderly. As stated earlier, the data on nutritional status of the study participants were unavailable. On the other hand, albumin and triglyceride, which are accepted indirect markers of nutritional status among community dwelling subjects, were found to independent factors for the

presence of NAFLD. These current findings suggest that long-term undernutrition in patients with diverticulosis and/or overnutrition of study participants without diverticulosis might influence the study's results. The lower probability of NAFLD in patients with diverticulosis might not be an indicator of a state of wellness, but a sign of undernutrition. Further prospective studies are required to assess the relationship between NAFLD, obesity, nutritional status and diverticulosis in older subjects.

Previous studies have investigated the frequencies of several metabolic syndrome-related disorders in patients with diverticular disease and the influence of these disorders on different subgroups of colonic diverticular disease. For example, a study conducted in Saudi Arabia found the prevalence of DM, HT and dyslipidaemia among patients with diverticulosis were 63%, 44% and 22%, respectively; and advanced age and HT were found to be independent risk factors for the presence of diverticulosis.[22] Another study conducted in Japan on patients with diverticulosis with a median age of 72 years found the prevalence of DM, HT and HL were 27%, 57% and 32%, respectively.[32] The results of these two studies are comparable with those of the current study. Advanced age may be related to higher rates of these disorders, irrespective of the presence of diverticulosis. However, these reported disorders have been related to symptomatic complicated diverticular disease.[16]

In addition to the aforementioned limitations, this study had several other limitations. First, this retrospective case–control study was the subject of selection bias of both the cases and controls. The study excluded those patients with chronic liver disease, those who had disorders related to secondary hepatosteatosis and those who were taking medications that cause hepatosteatosis. Thus, the current findings cannot be generalized for all subjects over 65 years. Secondly, hepatosteatosis was diagnosed using ultrasonography. To avoid interobserver variability, the study enrolled only subjects who had a radiological assessment performed by the same radiologist. More convenient diagnostic tools, like computed tomography and magnetic resonance imaging, might be used to measure the hepatosteatosis grade and/or calculate the fat content of the liver. Thirdly, a more thorough nutritional assessment was hampered by the lack of data on detailed dietary history.

In conclusion, the current study demonstrated lower rates of hepatosteatosis among elderly patients with diverticulosis. High albumin and triglyceride levels in patients with normal colonoscopic findings may indicate NAFLD. Lower albumin and triglyceride levels in conjunction with the presence of diverticulosis might be signs of undernutrition in the elderly. Further studies are needed to explain the effects of nutrition on diverticulosis and hepatosteatosis in older subjects.

Declaration of conflicting interest

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