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Comparison of ultrasonographic and laboratory findings of acute cholecystitis between elderly and nonelderly patients

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Background/aim: The incidence of acute cholecystitis (AC) increases with age, and aging is also one of the poor prognostic factors. Aging is related to altered physiology, so diseases may show different characteristics in elderly patients. We aimed to investigate the differences between the main characteristic features of AC in elderly and nonelderly patients.

Materials and methods: In this retrospective study, patients who had a diagnosis of AC were included and divided into two groups of people aged <65 years or ≥65 years. Laboratory and ultrasonographic findings related to AC were compared statistically between elderly and nonelderly patients.

Results: The data of 305 patients diagnosed with AC were recorded. Patients in the nonelderly group were more likely to be female, but in elderly patients the sex distribution was similar. There were no significant differences with respect to liver function tests and ultrasonographic findings at the time of admission between the elderly and nonelderly groups. However, the elderly group had a significantly higher rate of patients with an elevated white blood cell count and higher C-reactive protein values than the nonelderly group.

Conclusion: Aging is related to altered immunologic and pathophysiologic processes. Thus, age and baseline comorbidities influence overall mortality rates. Efforts should be made to understand disease mechanisms and minimize avoidable harms.

Key words: Aging physiology, systemic inflammatory response, gallbladder disease

1. Introduction

Acute cholecystitis (AC) refers to a gallbladder inflammation caused by gallbladder duct obstruction, bacterial infection, or chemical stimulation. It is one of the most frequently encountered clinical conditions of the abdomen (1).

Diagnostic criteria of AC include a local sign of inflammation such as Murphy's sign or right upper quadrant tenderness; a systemic sign of inflammation such as fever; elevated white blood cell count (WBC) or elevated C-reactive protein (CRP); and an imaging finding consistent with AC, which could include thickening of the gallbladder wall or pericholecystic fluid (2).

Although the course of AC may be self-limiting, sepsis, peritonitis secondary to gallbladder perforation, and cholecystoenteric fistulas may result from untreated or inadequately treated AC (3,4). The overall mortality rate of AC is approximately 0.6%.

The incidence of gallbladder disease increases with age, and aging is also one of the poor prognostic factors of the disease (2). Aging is related with altered physiology, so diseases may show different characteristics in elderly patients. Defining aging physiology and indicating its differences and similarities in different age groups are important steps for disease management in geriatric medicine. In this study, we aimed to investigate the differences between the main characteristic features of AC in elderly and non-elderly patients.

2. Materials and methods

This study was designed retrospectively and approved by the institutional review board. The inclusion criterion was having a diagnosis of AC. Patients admitted to the hospital with a diagnosis of AC between 1 January 2005 and 31 December 2014 were identified retrospectively by using

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the codes in the International Classification of Diseases, 10th Revision (ICD-10). All electronic and paper medical records of the patients were reviewed, and the diagnosis of AC was confirmed with a detailed evaluation of patient history, physical examination findings, laboratory analysis, and ultrasonography findings. Patients who did not have findings convenient with AC and patients with gallstone pancreatitis, coexisting hepatobiliary, or intestinal malignancy and autoimmune biliary disease were excluded from the study. Patients were then divided into two groups of individuals aged <65 years or ≥65 years.

The data of patients at the time of admission were recorded, which included basic demographic characteristics, laboratory measurements of liver function tests, white blood cell (WBC) count and C-reactive protein (CRP) levels, ultrasonographic findings indicative of gallbladder wall thickness, and the presence of gallstones. Laboratory measurements were stratified as normal or two-fold above the normal limit. An elevated WBC count was defined as a count of >10,000/mm^3 WBCs and an elevated CRP level was defined as >3 mg/dL CRP, both according to the Tokyo Guidelines (2).

All laboratory and ultrasonographic findings of AC were compared statistically between the two groups. Subgroup analyses by sex were also made in patients who were aged <65 years or ≥65 years.

2.1. Statistical analysis

The data were analyzed with SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA). The comparison between categorical variables was presented as the number and percentage of patients and carried out using a chi-square test. Pearson correlation analysis was done to test the correlation between independent variables. A two-sided P value of <0.05 was considered significant.

3. Results

The search for the ICD-10 code identified 573 patients who were diagnosed with AC in the emergency department or inpatient services between 1 January 2005 and 31 December 2014. Two hundred and sixty-eight patients were excluded from the study according to the exclusion criteria. The remaining 305 patients who had AC based on clinical, laboratory, and ultrasonographic criteria were included the final analysis.

The mean age of all cohorts was 58.9 ± 19.5 years (range: 18–96). The mean age of the elderly group was 77.6 ± 7.7 and the mean age of the nonelderly group was 44.7 ± 12.6. Patients in the nonelderly group were more likely to be female, but in elderly patients the sex distribution was similar. There were no significant differences with respect to liver function tests and ultrasonographic findings at the time of admission between the elderly and nonelderly groups. However, the elderly group had a significantly higher rate of patients who had an elevated WBC count and CRP values than the nonelderly group (Table 1; Figure).

In the elderly patients, there were no significant differences between male and female patients in all variables (Table 2).

In the Pearson correlation analysis, CRP values and WBC count were found to be statistically significant when associated with age (Table 3).

4. Discussion

In the present study, we showed the similarities and differences in demographic, laboratory, and imaging findings of AC between elderly and nonelderly patients. The sex distribution was significantly different between the groups, indicating that female and male patients had a similar rate in the elderly groups, while females had dominancy in the nonelderly group. Significant differences were also evident in WBC counts and CRP levels. The elderly group had a significantly higher rate of patients with elevated WBC counts and CRP values than the nonelderly group.

The management of biliary complications in elderly patients may pose a challenge. Increasing age independently predicts mortality and complications. Atypical or mild symptoms are more frequently present, and comorbidities influence the prognosis and the treatment options (5). Although recent advances in the treatment of acute biliary diseases have significantly improved the prognosis of patients, the morbidity and mortality rates of elderly patients have remained significantly higher than in nonelderly patients (6,7). Delayed surgery in acute conditions has higher risk in elderly patients comparing with nonelderly patients. AC has been recognized as life-threatening disease with poor prognosis in elderly patients (6,7) Therefore, defining the baseline features of this disease in elderly patients is important for emergent management. The majority of the studies conducted on elderly patients with AC have evaluated surgery methods or time. However, there are not enough data about the clinical features of AC in elderly patients (8,9).

We found some differences in demographic features between elderly and nonelderly patients with AC. For instance, AC is reported to be higher in the female population (10). However, we found that while the prevalence of female patients was higher than the prevalence of male patients in the nonelderly group, the distribution of sex was similar in the elderly group with AC. Supporting our data, McGillicuddy et al. found that there was no significant difference in sex distribution in elderly patients with AC (11). McKay et al. also reported similar results in elderly patients with AC who had undergone surgery (12).

Table 1. Comparison of demographic and clinical data of patients by age.

Parameters	Total	<65 years old (N: 174)	≥65 years old (N: 131)	P-value
Sex Male Female	 122 (40%) 183 (60%)	 61 (35.1%) 113 (64.9%)	 61 (46.6%) 70 (53.4%)	0.028
ALT Normal >2×	 96 (31.5%) 208 (68.2%)	 53 (30.5%) 121 (69.5%)	 43 (32.8%) 87 864.4%)	0.381
AST Normal >2×	 105 (34.4%) 200 (65.6%)	 60 (34.5%) 114 (65.5%)	 45 (34.4%) 86 (65.6%)	0.381
GGT Normal >2×	 90 (29.5%) 215 (70.5%)	 49 (28.2%) 125 (71.8%)	 41 (31.3%) 90 (68.7%)	0.455
ALP Normal >2×	 196 864.3%) 109 (35.7%)	 115 (66.1%) 59 (33.9%)	 81 (61.8%) 50 (38.2%)	0.407
Total bilirubin Normal Elevated	 165 (54.1%) 140 (45.9%)	 101 (58%) 73 (42%)	 64 (48.9%) 67 (51.1%)	0.130
Direct bilirubin Normal Elevated (>1.2 mg/dL)	 136 (44.6%) 169 (55.1%)	 85 (48.9%) 89 (51.1%)	 51 (38.9%) 80 (61.1%)	0.128
WBC count Normal Elevated (>10,500/mm^3)	 205 (67.2%) 100 (26.4%)	 128 (73.6%) 46 (26.4%)	 77 (58.8%) 54 (41.2%)	0.005
CRP Normal Elevated (>3 g/dL)	 160 (52.5%) 145 (47.5%)	 113 (64.9%) 61 (35.1%)	 47 (35.9%) 84 (64.1%)	<0.001
Gallbladder wall thickness Normal Elevated (≥4 mm)	 96 (31.5%) 209 (68.5%)	 60 (34.5%) 114 (65.5)	 36 (27.5%) 95 (72.5%)	0.176
Gallstone Present Absent	 246 (80.7%) 59 (19.3%)	 143 (82.7%) 30 (17.3%)	 103 (78%) 29 (22%)	0.193

ALT: Alanine aminotransferase, AST: aspartate aminotransferase, GGT: γ-glutamiltransferase, ALP: alkaline phosphatase, WBC: white blood cell count, CRP: C-reactive protein.

In the laboratory features, we found differences in systemic inflammatory markers between elderly and nonelderly patients. Elderly patients had significantly higher CRP values than nonelderly patients. in addition, While 41.2% of elderly patients had an elevated WBC count, 26.4% of nonelderly patients had an increased WBC count. This difference was also statistically significant. Similarly, Parker et al. also reported that 59% of elderly patients had an elevated WBC count in their study (13). These results may be caused by altered aging immunopathology. Although many inflammatory cells decrease with age, human aging is generally accompanied by elevated systemic inflammatory

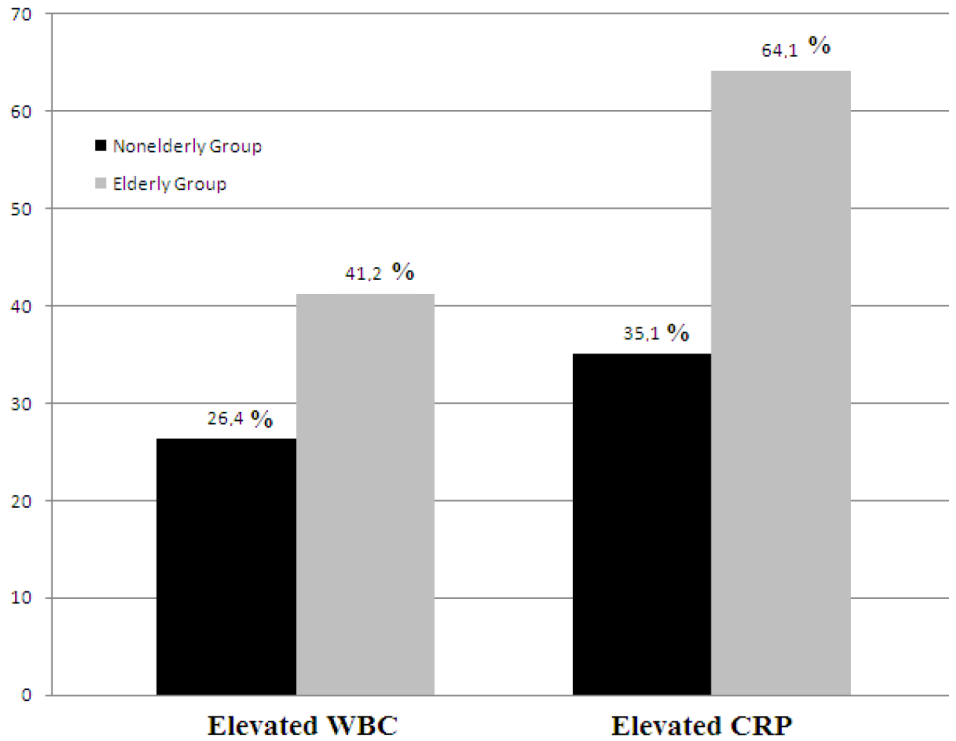

Figure. Differences in CRP and WBC values between groups.

conditions. Thus, inflammation-related biomarkers are powerful predictors of mortality in the elderly (14).

Older patients generally have more prolonged proinflammatory responses than nonelderly patients. This may reflect difficulties in clearing microbial agents or dysfunction in the attenuation of signaling by such counterregulatory cytokines such as IL-10. Studies have shown a similar pattern of excessive proinflammatory cytokine response to microbial mediators in aged mice (15,16). CRP is an acute-phase reactant and reflects an inflammatory state. The higher CRP values of elderly patients in our study may have resulted from these elevated systemic inflammatory conditions during aging.

On the other hand, natural killer (NK) cell populations gradually expand with age, and NK function is generally well preserved. However, there is some evidence that the lytic activity of these cells may be impaired with age (17,18). This relative loss of lytic activity is essentially compensated for by an expansion of NK cell populations in elderly persons and this may explain the higher WBC values in elderly patients with AC.

We did not find significant differences in the prevalence of increased gallbladder wall thickness. These data also support previous data presented by Fuks et al., who compared the intraoperative findings of young and elderly patients with AC (19).

In addition, aging is related with certain physiological changes in gastrointestinal system functions such as a decreased sensitivity of the gallbladder to cholecystokinin stimulation (20). Besides a changed gastrointestinal physiology, an increased status of oxidative stress over time and chronic exposure to infections may contribute to the higher inflammatory state in elderly patients with AC.

Some important limitations of this study must be acknowledged. First of all, this is a retrospective study from a single center, and the study was subjected to the limitations inherent to chart reviews and depended on the accuracy of the coded data. Because only hospital charts were reviewed, the data may give an incomplete picture of the overall clinical course of the patients. For example, the data did not capture the visits to the patients' family doctors or surgeons in an outpatient setting. Also, patients may have been seen in other hospitals, although interhospital movement is generally uncommon in this population. This study used administrative data that did not indicate the outcome results.

In conclusion, aging is related to altered immunologic and pathophysiologic processes. Thus, age and baseline comorbidities influence overall mortality rates, which are over 5% in AC and cholecystitis. Efforts should be made to understand disease mechanisms and minimize avoidable harms. Altered functions in elderly patients should be considered in treatment decisions that will have major influence on prognosis.

Table 2. Comparison of clinical data of patients by sex in patients above 65 years old.

Parameters	Male (N: 61)	Female (N: 70)	P-value
ALT Normal >2×	 17 (27.9%) 44 (72.1%)	 26 (37.1%) 44 (62.9%)	0.253
AST Normal >2×	 17 (27.9%) 44 (72.1%)	 27 (38.6%) 43 (61.4)	0.311
GGT Normal >2×	 15 (24.6%) 46 (75.4%)	 26 (37.1%) 44 (62.9%)	0.121
ALP Normal >2×	 35 (57.4%) 26 (42.6%)	 47 (67.1%) 23 (32.9%)	0.478
Total bilirubin Normal Elevated	 25 (41%) 36 (59%)	 39 (55.7%) 31 (44.3%)	0.384
Direct bilirubin Normal Elevated (>1.2 mg/dL)	 20 (32.8%) 41 (67.2%)	 31(44.3%) 39 (55.7%)	0.412
WBC Normal Elevated (>10,500/mm^3)	 40 (65.6%) 21 (34.4%)	 37 (52.9%) 33 (47.1%)	0.097
CRP Normal Elevated (>3 g/dL)	 24 (38%) 37 (62%)	 23 (32.9%) 47 (67.1%)	0.571
Gallbladder wall thickness Normal Elevated (≥4 mm)	 16 (40%) 48 (60%)	 20 (40%) 50 (60%)	0.858
Gallstones Present Absent	 44 (72.1%) 17 (27.9%)	 59 (83.1%) 12 (16.9%)	0.096

ALT: Alanine aminotransferase, AST: aspartate aminotransferase, GGT: γ-glutamiltransferase, ALP: alkaline phosphatase, WBC: white blood cell count, CRP: C-reactive protein.

Table 3. Correlations between age and WBC and CRP values.

		WBC	CRP
Age	Pearson correlation	0.223**	0.276**
	P-value	<0.001	<0.001

**Correlation is significant at the 0.01 level (2-tailed).
WBC: White blood cell count, CRP: C-reactive protein.

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