Response to: Serum Paraoxonase and Malondialdehyde Levels in Asymptomatic Cholelithiasis

Sir,

We thank Agilli et al.[1] for commenting on our manuscript.[2] We would like to respond to their concerns.

Agilli et al.[1] suggested to use erythrocyte sedimentation rate (ESR) and complete blood count, in addition to C-reactive protein (CRP) to assess inflammatory status. Osei-Bimpong et al.[3] suggested that ESR and CRP are equally useful and reliable tests for screening and showed that after 40 years of age, there is an age-related elevation of ESR, increasing steadily, especially after age 60 years. CRP is also affected by age, but to a much lesser extent.[3] The mean age of our cholelithiasis group was 51 years and control group was 57 years, and it is clear that CRP reflects inflammatory status much better than ESR in this age group.[3] In 1992, the combination of abdominal ultrasonography and measurement of CRP was recommended in the routine evaluation of all patients with suspected acute cholecystitis.[4] In recent studies, elevated CRP has been found to have a high predictive value in predicting gangrenous cholecystitis[5] and conversion from laparoscopic to open cholecystectomy.[6] Agilli et al. refer to the study by Kono et al.[7] to criticize our use of CRP. Kono et al. performed a study on 11 children and showed that some of the studied 3 months to 3-year-old children with bacterial infection did not mount an elevated CRP level in response to infection.[7] Our study population of adults and those small children are quite different patient groups. Therefore, we believe that utilization of CRP level was enough to exclude both control and cholelithiasis subjects with signs of inflammation and the determination of the study and control groups was probably reliable.

The second issue raised by Agilli et al. is about methodology.[1] They point to inaccuracy of thiobarbituric acid reactive substances (TBARS) assay on measuring malondialdehyde (MDA) level and suggest using a chromatographic assay. TBARS assay detects oxidized lipids, saturated and unsaturated aldehydes, sucrose, urea, and various chromogens in addition to MDA, causing overestimation of MDA.[8] As subjects with renal and endocrine diseases were excluded from the study, we believe that the observed difference in TBARS assay reflects the difference in MDA levels and doubt that other chromogens and other TBARS caused the observed difference. In any case, we agree that a chromatographic assay is superior to TBARS assay. We suggest that further studies should employ a chromatographic assay in determining MDA.

The third issue is about the errors in tables. We thank Agilli et al. for pointing out several errors in Table 1. Those were corrected in the revised table 1 presented with this communication. There was an error in the mean age of control subjects. The mean age of the controls was 56.93 years and was significantly higher than the mean age of the subjects with cholelithiasis (P = 0.016). There was an error in the calculation of low-density lipoprotein cholesterol (LDL-C) by the Friedewald formula in healthy controls. The correct calculation of low-density lipoprotein cholesterol (LDL-C) by the Friedewald formula would have been 35.81 IU/L. The mean GGT level of control subjects was reported wrong and should have been 25.48 IU/L. The mean GGT level of cholelithiasis subjects was reported wrong and should have been 35.81 IU/L. The mean GGT level of control

Table 1: Comparison of clinical and biochemical parameters between healthy control and cholelithiasis group

| Variables              | Healthy control (n=40) | Cholelithiasis (n=80) | P      |
|------------------------|------------------------|-----------------------|--------|
|                        | Mean                   | SD                    | Mean   | SD   |        |
| Age (years)            | 56.93b                 | 11.73                 | 50.56  | 14.28| 0.016a |
| Glucose (mg/dL)        | 95.70                  | 10.00                 | 101.70 | 21.37| 0.218  |
| T.Chol (mg/dL)         | 179.45                 | 20.05                 | 200.15 | 39.91| 0.001  |
| HDL-C (mg/dL)*         | 49.35                  | 6.74                  | 41.18  | 14.18| 0.001  |
| LDL-C (mg/dL)*         | 100.86                 | 23.96                 | 124.26 | 31.62| 0.049  |
| Triglyceride (mg/dL)*  | 146.20                 | 14.71                 | 159.34 | 54.15| 0.452  |
| hsCRP (mg/dL)*         | 0.31                   | 0.11                  | 0.35   | 0.21 | 0.764  |
| ALT (IU/L)             | 33.60                  | 6.61                  | 34.15  | 19.05| 0.335  |
| AST (IU/L)             | 30.00                  | 6.75                  | 25.48  | 12.50| 0.000a |
| GGT (IU/L)             | 41.70                  | 4.05                  | 35.81  | 17.00| 0.002a |
| MDA (nmol/mL)          | 3.62                   | 1.44                  | 5.64   | 1.89 | 0.000  |
| PON-1* (IU/L)          | 441.20                 | 47.02                 | 346.07 | 109.83| 0.001  |
| Gender                 |                        |                       |        |      |        |
| Female                 | 25                     | 62.5                  | 55     | 68.8 | 0.494  |
| Male                   | 15                     | 37.5                  | 25     | 31.3 |        |

SD: Standard deviation. T.Chol: Total cholesterol. HDL-C: High-density lipoprotein cholesterol. LDL-C: Low-density lipoprotein cholesterol. hsCRP: Highly sensitive C-reactive protein. ALT: Alanine transaminase. AST: Aspartate transaminase. GGT: Gamma-glutamyltransferase. MDA: Malondialdehyde. PON-1: Paraoxonase. *Student’s t test. *Mann–Whitney U test. *Chi-square test. *The correct value that replaced the erroneous value from table 1 of our previously published article[2]
subjects was significantly higher than the mean GGT level of cholelithiasis subjects ($P = 0.002$). These corrections are shown in the revised table 1 in this communication. The following corrections need to be done in the text of the manuscript that pertains to the revised table 1. In the Abstract, in the first sentence of the Patients and Methods section, there is an error in the number and age of subjects without cholelithiasis. The correct numbers are 25 women, 15 men, mean age 57 years, and SD 12 years. The second sentence of the Results section should be as follows: “Twenty-five women (62.5%) and 15 men (37.5%) with a mean age ± SD of 56.93 ± 11.73 years were included in the control group and control subjects were significantly older than cholelithiasis subjects ($P = 0.016$).” These errors were also present in table 1 of another publication of ours that derived data from the same subject group.\textsuperscript{[9]} This should have been mentioned in the Acknowledgements as well as the editing and submission assistance by Ahmet Selcuk Can (the third author of this letter). Aytaç Atamer and Yıldız Atamer is responsible for the integrity of the published data.\textsuperscript{[2]} Ahmet Selçuk Can is responsible from editing and submission of the published manuscript\textsuperscript{[2]} and writing and submission of this letter. We agree with Agilli et al.\textsuperscript{[1]} and accept that several errors make the published study\textsuperscript{[2]} unreliable.

The fourth issue is about the interpretation of our study results. Previous studies show that the metabolic syndrome is one of the risk factors for cholelithiasis.\textsuperscript{[10,11]} We cannot differentiate from our data if lower paraoxonase activity and higher MDA levels we observed in cholelithiasis subjects compared with controls are due to cholelithiasis \textit{per se} or the metabolic syndrome. Our study shows that subjects with cholelithiasis and with the components of the metabolic syndrome have evidence of more lipid peroxidation and less antioxidant capacity than subjects with cholelithiasis and without the components of the metabolic syndrome.\textsuperscript{[2]}

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Aytaç Atamer\textsuperscript{1,2}, Yıldız Atamer\textsuperscript{1}, Ahmet S. Can\textsuperscript{1}

\textsuperscript{1}Termal Vocational School, Yalova University, Yalova, \textsuperscript{2}Division of Gastroenterology, Department of Internal Medicine, Ministry of Health Haydarpasha Numune Training and Research Hospital, Istanbul, Turkey

E-mail: selcukcan@endokrinoloji.com

REFERENCES

1. Agilli M, Aydin FN, Aydin I. Serum paraoxonase and malondialdehyde levels in asymptomatic cholelithiasis. Saudi J Gastroenterol 2014;20:203-4.
2. Atamer A, Kurdas-Ovunc AO, Yesil A, Atamer Y. Evaluation of paraoxonase, malondialdehyde, and lipoprotein levels in patients with asymptomatic cholelithiasis. Saudi J Gastroenterol 2014;20:66-73.
3. Osei-Bimpong A, Meek JH, Lewis SM. ESR or CRP? A comparison of their clinical utility. Hematology 2007;12:353-7.
4. Juvonen T, Kiviniemi H, Niemela O, Kairaluoma ML. Diagnostic accuracy of ultrasonography and C reactive protein concentration in acute cholecystitis: A prospective clinical study. Eur J Surg 1992;158:365-9.
5. Mok KW, Reddy R, Wood F, Turner P, Ward JB, Pursnani KG, et al. Is C-reactive protein a useful adjunct in selecting patients for emergency cholecystectomy by predicting severe/gangrenous cholecystitis? Int J Surg 2014;12:649-53.
6. Wevers KP, van Westreenen HL, Patijn GA. Laparoscopic cholecystectomy in acute cholecystitis: C-reactive protein level combined with age predicts conversion. Surg Laparosc Endosc Percutan Tech 2013;23:163-6.
7. Kono T, Otsuka M, Ito M, Misawa M, Hoshioka A, Suzuki M, et al. Negative C-reactive protein in children with bacterial infection. Pediatr Int 1999;41:496-9.
8. Moselhy HE, Reid RG, Yousef S, Boyle SP. A specific, accurate, and sensitive measure of total plasma malondialdehyde by HPLC. J Lipid Res 2013;54:852-8.
9. Atamer A, Ovint AO, Yesil A, Atamer Y. Evaluation of leptin and insulin resistance in patients with cholelithiasis. Indian J Biochem Biophys 2013;50:266-72.
10. Shebl FM, Andreotti G, Meyer TE, Gao YT, Rashid A, Yu K, et al. Metabolic syndrome and insulin resistance in relation to biliary tract cancer and stone risks: A population-based study in Shanghai, China. Br J Cancer 2011;105:1424-9.
11. Kairala LY, Qiao QH, Zhang SC, Chen YH, Chao GQ, Fang LZ. Metabolic syndrome and gallstone disease. World J Gastroenterol 2012;18:4215-20.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.