

## LETTER TO THE EDITOR

# The authors reply: Re: Yamamoto R, Sugiura T, Ashida R, Ohgi K, Yamada M, Otsuka S, and Uesaka K. Prognostic value of carbohydrate antigen 19-9 and the surgical margin in extrahepatic Cholangiocarcinoma. *Ann Gastroenterol Surg*. 2022;6:307–315

Dear Editor,

We would like to respond to the Letter to the Editor by Zaleskis et al.,<sup>1</sup> which comments on our original article "Prognostic value of carbohydrate antigen 19-9 and the surgical margin in extrahepatic cholangiocarcinoma" in *Ann Gastroenterol Surg*. They proposed using the specific growth rate (SGR) of the perioperative carbohydrate antigen 19-9 (CA19-9) values rather than the absolute value of CA19-9 for predicting the prognosis of extrahepatic cholangiocarcinoma.<sup>2</sup>

We calculated the SGR of the perioperative CA19-9 values as follows:  $SGR = \ln(\text{postoperative CA19-9} / \text{preoperative CA19-9}) / \text{interval days}$ . The median SGR of CA19-9 was  $-0.020$  with an interquartile range from  $-0.040$  to  $-0.005$ . We divided the SGR values into four groups: group A ( $SGR < -0.06$ ), group B ( $SGR \geq -0.06$  to  $< -0.03$ ), group C ( $SGR \geq -0.03$  to  $< 0$ ), and group D ( $SGR \geq 0$ ). Table 1 shows the characteristics according to the SGR value. The preoperative CA19-9 value was significantly higher in group A and lower in group D in comparison to the other groups. The postoperative CA19-9 was significantly higher in group D in comparison to the other groups.

The R1 resection rate and locoregional recurrence rate did not differ to a statistically significant extent among the groups. The distant recurrence rate in group C was significantly lower in comparison to groups A and B. The overall survival of the groups did not differ to a statistically significant extent (Figure S1).

In contrast to Zaleskis's expectation, the SGR value of the perioperative CA19-9 values was not associated with the prognosis of extrahepatic cholangiocarcinoma. The SGR has a greater negative value when the perioperative CA19-9 reduction rate was greater. Patients with greater negative SGR values had higher preoperative CA19-9 values, so greater negative SGR values were not associated with a good prognosis. Group C had low preoperative and postoperative CA19-9 values, which might account for the lower rate of distant recurrence. On the other hand, an increase in the perioperative CA19-9 value results in a positive SGR value. Group D has positive SGR values, but the preoperative and postoperative CA19-9 values were not high; thus, positive SGR values were not associated with a poor prognosis.

**TABLE 1** Characteristics according to the specific growth rate value

	Group A (n = 51)	Group B (n = 90)	Group C (n = 179)	Group D (n = 70)
Preoperative CA19-9 (U/mL) <sup>a</sup>	749 (307–1984)	105 (59–253)	24 (16–57)	13 (8–29)
Postoperative CA19-9 (U/mL) <sup>a</sup>	13 (7–37)	11 (6–20)	12 (8–20)	26 (15–72)
R1 resection	8 (16)	11 (12)	16 (9)	14 (20)
Locoregional recurrence	3 (6)	12 (13)	27 (15)	11 (16)
Distant recurrence	35 (69)	52 (58)	69 (39)	32 (46)
Overall survival (months) <sup>b</sup>	40 (31–57))	39 (32–59)	54 (45–82)	42 (33–78)

Note: Values in parentheses are percentages unless otherwise indicated.

Abbreviation: CA19-9, carbohydrate antigen 19-9.

<sup>a</sup>Values are median (interquartile range).

<sup>b</sup>Values are median (95% confidence interval).

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The SGR value of the perioperative CA19-9 value was not related to the prognosis of extrahepatic cholangiocarcinoma. As we showed in our original article, the assessment of the absolute value of CA19-9 is important for predicting the prognosis of extrahepatic cholangiocarcinoma.<sup>3</sup>

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#### CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest for this article.

#### ETHICAL APPROVAL

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Animal Studies: N/A.

Ryusei Yamamoto

Teiichi Sugiura 

Ryo Ashida 

Katsuhisa Ohgi

Mihoko Yamada

Shimpei Otsuka

Katsuhiko Uesaka

Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer  
Center, Shizuoka, Japan

#### Correspondence

Teiichi Sugiura, Division of Hepato-Biliary-Pancreatic  
Surgery, Shizuoka Cancer Center, 1007 Shimo-Nagakubo,  
Sunto-Nagaizumi, Shizuoka 411-8777, Japan.

Email: [t.sugiura@scchr.jp](mailto:t.sugiura@scchr.jp)

#### ORCID

Teiichi Sugiura  <https://orcid.org/0000-0001-7163-4084>

Ryo Ashida  <https://orcid.org/0000-0001-8388-0135>

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.