



Fig. 1. Liver histopathological findings. A) Cholestasis: Bile pigments within hepatic parenchyma (40X magnification, hematoxylin-eosin staining). B) Lobular hepatitis: Hepatic lobules show ballooning of hepatocytes with lymphocytic and eosinophilic infiltrates (40X magnification, hematoxylin-eosin staining). C) Marked portal inflammation involving lymph plasma cells and few eosinophils (40X magnification, hematoxylin-eosin staining). D) Mild to moderate fibrosis (10X magnification, trichrome staining).

only few cases of autoimmune hepatitis have been reported following COVID-19 vaccination [6], this was the first case report of an autoimmune hepatitis after Sinopharm COVID-19 vaccination. Similar to most previous reports, our patient was also a female, but she was younger than other patients described in previous reports. Besides, the interval until the emergence of vaccine-related complications was shorter in our patient compared to previous reports.

In rare cases, COVID-19 vaccines may act as a trigger or activator of autoimmune hepatitis by stimulating the immune system; therefore, this condition should be considered in the differential diagnosis of acute hepatitis of unknown etiology.

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The impact of the COVID-19 pandemic on adherence to first-round colorectal cancer screening program: a public health issue

To the Editor,

Adherence to a colorectal cancer (CRC) screening program is a long-lasting challenge. Different patient- and system-level factors have been identified in the past [1], to which the negative impact of the COVID-19 pandemic should be added. Indeed, many countries temporarily suspended their cancer screening activities in the early months of the emergency [2], contributing to the idea spreading that undergoing cancer

screening can be postponed. As a result, a significant decrease in the participation rate to these programs was observed worldwide in 2020 and 2021, with consequences yet to be determined [3].

In our center, the CRC screening program was suspended for three months (March-May 2020) and was resumed in June, when all subjects not invited during the suspension period were contacted. We report data on adherence and endoscopic findings in subjects who tested positive for the fecal immunochemical test (FIT) and eventually underwent colonoscopy, comparing data from 2018-2019 (before the pandemic) to 2020-2021 (during the pandemic) and focusing on individuals who accepted to enter our program for the first time.

A total of 627 subjects with FIT-positive results at first round underwent colonoscopy during the study period (Table I). Despite a similar invitation rate, there was a distinct reduction in the number of participants during the pandemic period (455 vs. 172 subjects). This finding was associated with a significantly lower elapse time between FIT and colonoscopy in 2020-2021, with an increased percentage of subjects who underwent colonoscopy within 30 days. No other difference emerged. However, in line with the literature [4], the fecal hemoglobin concentrations were significantly higher in individuals with advanced colorectal neoplasia than in those with non-advanced neoplasia (411 vs. 241 ng/mL, $p < 0.001$), as well as in cases with a distal lesion compared to subjects with a proximal lesion (363.5 vs. 221.5 ng/mL, $p < 0.001$).

Our data found that the COVID-19 pandemic did not affect the quality of the endoscopic visits, despite the work-related stress of physicians during the pandemic situation.

Indeed, the endoscopic performance and detection of advanced neoplastic lesions remained unchanged. In contrast, compared to previous years, fewer people entered the CRC screening program for the first time in 2020, and only a partial catch-up was observed in 2021. Reasons underlying non-adherence to CRC screening are different, including socioeconomic, ethnic and sociological influences. In addition, restrictions of mobility and fear of becoming infected with colonoscopy could have been other barriers during the COVID-19 pandemic. However, it has been demonstrated that initial participation is a predictor for continuous participation in population-based CRC screening [5]. Therefore, effective strategies aimed at restoring the importance of participating in CRC screening programs as soon as the subject become eligible should be implemented. Particularly, to minimize the long-term impact of the COVID-19 pandemic and avoid a public health crisis, we should reach out to the individuals that declined to enter the program for the first time in 2020 and 2021 through the development of targeted initiatives aimed at improving their knowledge and awareness of the benefits of participating in CRC screening programs and by providing them logistical support.

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Table I. Demographic and clinical characteristics of the participants (N=627) by year.

	2018 (N = 240)	2019 (N = 215)	2020 (N = 48)	2021 (N = 124)	p
Gender N, %					0.52
Female	135 (56.3)	116 (54.0)	22 (45.8)	63 (50.8)	
Male	105 (43.8)	99 (46.0)	26 (54.2)	61 (49.2)	
Age, median (IQR)	52.1 (50.2-60.6)	51.2 (50.4-52.4)	50.6 (50.3-52.2)	52.4 (50.6-53.4)	<0.001
Haemoglobin concentration (ng/mL), median (IQR)	239.5 (150-635.5)	299 (159-791)	273.5 (136.5-589)	248.5 (141-513.5)	0.21
Colonoscopy finding N, %					0.63
Normal finding or non-neoplastic lesion	191 (79.6)	169 (78.6)	35 (72.9)	93 (75.0)	
Colorectal cancer or advanced adenoma	49 (20.4)	46 (21.4)	13 (27.1)	31 (25.0)	
Lesion site N, % (N=364)					0.40
Proximal colon	23 (9.6)	21 (9.8)	5 (10.4)	18 (14.5)	
Distal colon	74 (30.8)	62 (28.8)	18 (37.5)	42 (33.9)	
Lesion dimension (mm), median (IQR) (N = 364)	9 (5-18)	8 (5-15)	10 (5-15)	10 (3.5-12)	0.83
Days elapsed from the FIT to colonoscopy, median (IQR) (N = 624)	52 (36-74.5)	40 (27-54)	35 (20.5-45)	47 (34-77)	<0.001
Colonoscopy completion N, %					0.93
Complete	229 (95.4)	206 (95.8)	45 (93.8)	119 (96.0)	
Incomplete	11 (4.6)	9 (4.2)	3 (6.3)	5 (4.0)	
Positive predictive value, % (95% CI)	20.4 (15.5-26.1)	21.4 (16.1-27.5)	27.1 (15.3-41.9)	25.0 (17.7-33.6)	0.63
Proportion of subjects undergoing colonoscopy within 30 days from FIT positivity, % (95% CI)	14.6 (10.4-19.7)	31.2 (25.0-37.8)	41.7 (27.6-56.8)	20.2 (13.5-28.3)	<0.001

IQR: interquartile range; FIT: faecal immunochemical test; CI: confidence interval. Chi-square test was used for categorical data and Kruskal-Wallis test was used for continuous data.

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Ageing and comorbidities in humans with anti gliadin antibodies

To the Editor,

We read with interest the paper *Clinical Relevance of Anti-Gliadin Seropositivity in the Ageing Population: A Long-term Follow-up Study* by Ruuskanen et al. [1] recently published in your journal. The authors reviewed the medical records of human subjects with anti gliadin antibodies (AGA) during long term follow-up. They evaluated 182 subjects aged 64-88 years (median 76 years) who were AGA-positive or negative after more than 12 years from the first AGA assessment. Only 1 patient tested genetically positive for celiac disease. The authors investigated autoimmune, neurological, psychiatric and oncological comorbidities at the end of the follow-up. They reported, as expected, ageing-associated comorbidities. However, their prevalence was not statistically different between the AGA positive versus AGA negative group, except for neurological diseases ($p=0.017$). These conditions included stroke, Alzheimer disease and polyneuropathies. If only new cases of neurological diseases, diagnosed during the follow-up are counted, the significance vanished. These data suggest that the elderly with AGA antibodies but with negative genetic tests for celiac disease have more neurological comorbidities than those with negative AGA suggesting that these neurological diseases were present at the baseline. We would like to know if in the patients with neurological disorders, the patients were also stratified according to specific pathologies, and if there were differences between AGA positive and AGA negative cases. It would be interesting to know if dementia or

polyneuropathies or strokes are more frequent in one group than in the other, rather than in the neurological comorbidities taken together. On the other hand, we suggest that in a future approach, the authors will search for the role of the alteration of circadian rhythm in the elderly; this factor may influence their neurological and mental health [2, 3]. The same is true for some autoimmune conditions, some of which have been investigated in this study, which can also be influenced by the circadian rhythmicity [2, 4]. Another putative mechanism of the link between occurrence of neurological conditions and gut conditions is of course microbiota [5], which was not evaluated at the baseline in this population.

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Reply,

To the Editor,

We appreciate the comment by Dumitrascu DI and Popa-Wagner A [1] with regard to our paper [2]. We compared mortality and morbidity of persistently AGA-positive and AGA-negative subjects during a long-term follow-up of 12-13 years since the initial antibody analysis. We found cumulative prevalence of neurological diseases more frequent in the AGA-negative group in this register-based study. We had, however, clinically examined the whole AGA-negative group but only about one third of the AGA-positive group in our earlier study [3], which probably caused bias to our results. Most common