

Pre-Endoscopy real-time PCR testing for SARS-CoV2 does not reduce health care workers infection and is associated with a higher reduction of endoscopic activity in an outpatient setting

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Abstract

Objective: The role of pre-procedure SARS-CoV2 testing in digestive endoscopy is still debated. AGA guidelines recommend against pre-procedure testing considering low prevalence of SARS-CoV2 infection in the general population and low incidence of infection among endoscopy units Health Care Workers (HCWs). However, no studies have compared pre-procedure testing associated to symptom screening vs. symptom screening alone in reducing the risk of infection for HCWs. Main aim of the present study is to compare the risk of infection for HCWs in different Endoscopy Units adopting different pre-endoscopy screening and operating in two nearby hospital of the same region in Northern Italy in pre-vaccination period. For outpatients in the Endoscopy Unit of Trento (Unit 1) only pre-procedure symptom screening was performed, while in the Endoscopy Unit of Bolzano (Unit 2) pre-procedure symptom screening and negative pre-procedure real-time PCR were requested. Secondary aims were to assess the impact of pre-procedure real-time PCR testing on endoscopic activity and diagnostic delay.

Design: Retrospective data collection on a prospectively maintained database was performed, including outpatient endoscopy procedures performed between June 1st 2020 and February 28th 2021 in Unit 1 and Unit 2.

Results: No differences in terms of infection rate in HCWs have been identified in Unit 1 and Unit 2 (9.0 vs. 19.3% P=0.2) over a nine-month period. Moreover, in the unit performing pre-procedure real-time PCR before endoscopy a significantly higher reduction in endoscopic activity has been recorded (61.9% vs. 53.4%; P<0.01). In patients with positive real-time PCR, endoscopy was performed with a mean delay of 61.7 days (range 9-294) and 22.5% of them were lost at follow-up and did not undergo any endoscopic procedure in the following 12 months.

Conclusions: This study supports the AGA recommendation suggesting that pre-endoscopy real-time PCR is an expensive and time-consuming procedure without proven benefits in an outpatient setting. (*Acta gastroenterol. belg.*, 2022, 85, 581-585).

What is already known on this topic

- AGA guidelines recommend against pre-procedure testing considering low prevalence of SARS-CoV2 infection in the general population, low incidence of infection and high vaccination rate among endoscopy units Health Care Workers (HCWs)
- No studies have compared pre-procedure testing associated to symptom screening vs. symptom screening alone in reducing the risk of infection for HCWs

What this study adds

- The present study confirms the hypothesis that real-time PCR pre-procedure testing in outpatient endoscopy does not reduce the risk of infection in HCWs
- Real-time PCR pre-procedure testing might be related to a higher reduction in endoscopic activity

How this study might affect research, practice or policy

- Pre-procedure real time PCR has no proven benefits in endoscopy units regardless of vaccination
- Data produced during pre-vaccination period might be extremely useful in countries with low vaccination rate and might give additional information in case of development of new SARS-CoV-2 variants

Objectives

The role of routine pre-procedure testing for SARS-CoV2 in patients undergoing upper or lower endoscopy is still debated. No homogeneous strategy has been established and different approaches have been proposed to reduce the risk of infection for health care workers (HCWs) of endoscopy units. In previous recommendations published in 2020, AGA recommended implementation of pretesting strategy in areas with prevalence of asymptomatic SARS-CoV-2 infection higher than 2% (1). However, a recent update has recommended against pre-procedure testing for SARS-CoV2, considering high vaccination rate in HCWs, low prevalence of asymptomatic SARS-CoV2 infection among patients referred for endoscopic procedures and the low risk of SARS-CoV2 transmission reported in endoscopy units (2). In detail, as reported in the AGA

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guidelines, across 12 studies on patients undergoing endoscopy, asymptomatic prevalence of SARS-CoV2 infection ranged from 0.0% to 1.5%, but most studies reported a range from 0% to 0.5% (3-14). Moreover, few studies reported infection rates for HCWs ranging from 0% to 4.0% (15,16). However, to date no studies comparing pre-procedure testing in combination with symptom screening vs. symptom screening alone on HCWs infections have been published (2). Furthermore, studies evaluating the risk of infection in HCWs in pre-vaccination period are still lacking, although their results might be useful in giving additional information for the management of endoscopy units, especially in countries with low vaccination coverage or in case of development of new virus variants. Finally, considering the high prevalence of SARS-CoV2 infection despite vaccination, it might contribute to a better definition of the real risk of infection in endoscopy units HCWs.

Design

Aim of the present study is the evaluation of HCWs infection rate, comparing two different endoscopy units of Northern Italy in a pre-vaccination period, namely the Endoscopy Unit of Trento (Unit 1) and the Endoscopy Unit of Bolzano (Unit 2). The two Units, located in the same region of Northern Italy (Region of Trentino-Alto Adige), only 55 Km away from each other, have similar endoscopic activity (around 10.000 endoscopic procedure per year in pre-SARS-CoV2 period) and comparable number of HCWs. The two Units adopted different pre-procedure strategies for outpatient endoscopy starting from June 1st 2020. Unit 1 performed symptom screening, while Unit 2 required symptom screening and pre-procedure real-time PCR testing performed within 48 hours before endoscopy. Both Units adopted similar protective measures and personal protective equipment (PPE). Finally, both units, as recommended by their hospitals, required real-time PCR before hospitalization.

Endoscopic procedures, patient's demographics, clinical data, HCWs infections were retrospectively evaluated from a prospective maintained database between June 1st 2020 and February 28th 2021. Patients signed a consent permission form before real-time PCR and endoscopy procedure. Moreover, they were actively informed that pre-procedure testing was experimentally introduced in order to develop preventive strategies to reduce the risk of infection of HCWs and the overall SARS-CoV-2 diffusion. No additional patients and the public involvement was planned.

The period was defined by the following reasons: first, from June 1st 2020 the Unit 2 started the routinely use of real-time PCR before outpatient endoscopy in addition to symptom questionnaire; second, after February 28th 2021, all the HCWs of the two units completed vaccination.

All consecutive outpatient endoscopic procedures were included. Exclusion criteria were inpatient procedures and patients with age < 18 years.

Main outcome is the comparison of infection rate of HCWs in both endoscopy units over the nine-month period. Secondary outcome is the impact of the two different pre-procedure strategies on endoscopic activity in terms of number of performed endoscopies and diagnostic delay.

Fisher's exact test and *chi-square* test were used for continuous and categorical data, respectively. A *P*-value <0.05 was considered significant. Mean and standard deviation are reported. Statistic was processed using the SPSS 17 statistical program (SPSS Inc., Chicago, IL, USA). The study was approved by the local ethical committee (protocol number 102-2021).

Results

1. HCWs Infections

During the considered period, 33 HCWs were working full time in Unit 1, with a mean age of 45.5±9.5 years (13 physicians, 16 nurses and 4 health care assistants). Ten were males (30.3%) and 23 females (69.7%). Three (9%) developed SARS-CoV2 infection diagnosed with positive real-time PCR test, during the study period, 1 nurse, and 2 health care assistants, respectively. All the infections were asymptomatic and diagnosed in February 2021.

During the considered period, 31 HCWs were working full time in Unit 2, with a mean age of 47.7±10.5 years (14 physicians, 13 nurses, and 4 health care assistants). Sixteen were males (51.6%) and 15 females (48.4%). Six workers (19.3%) developed a SARS-CoV2 infection, diagnosed with real-time PCR test during the study period: 2 physicians, 3 nurses, and 1 health care assistant. Among them, 2 HCWs had symptomatic infection without need of hospitalization, while the other 4 were asymptomatic. Five infections were diagnosed between November and December 2020, and one in February 2021.

There were no significant differences in age or gender distribution of HCWs between Unit 1 and Unit 2. Moreover, the difference in terms of SARS-CoV2 infection between the two units was not statistically significant (Unit 1 9% vs. Unit 2 19.3%; *P*=0.2). HCWs demographics and infections are reported in Table 1.

2. Endoscopic Activity

During the study period (COVID), 5763 endoscopic procedure have been performed in an outpatient setting. Three-thousand-three-hundred-seventy endoscopic outpatient procedures (41.5%) have been performed at Unit 1 and 2393 (51.5%) at Unit 2. In the same period of the pre-SARS-CoV2 pandemic (pre-COVID), between June 1st 2019 and February 28th 2020, the two units performed 13506 endoscopic procedures, with an overall decrease of 57.3% in COVID period (Table 2.).

The overall reduction in endoscopic activity was 53.4% and 61.9%, respectively for Unit 1 and Unit 2. This

Table 1.

	Total	Unit 1	Unit 2	P
HCWs nr:	64	33	31	
physicians nr:	27	13	14	NS (0.8)
nurses nr:	29	16	13	NS (0.6)
health care workers nr:	8	4	4	NS (>.99)
Male nr. (%)	26 (40.6)	10 (30.3)	16 (51.6)	NS (0.12)
Age, yrs (SD)	46.4 (10.5)	45.5 (9.5)	47.7 (10.5)	NS (>.99)
Infections nr. (%)	9 (14.1)	3 (9%)	6 (19.3)	NS (0.2)

Table 2.

	Upper Endoscopy	Lower Endoscopy	EUS	total
Unit 1 pre-COVID	2607	4398	228	7233
Unit 1 COVID	1192	2062	116	3370
Unit 2 pre-COVID	1804	4336	133	6273
Unit 2 COVID	743	1587	63	2393

Table 3.

Reduction of endoscopic activity	Unit 1	Unit 2	P
Total	53.4	61.9	<0.01
Upper endoscopy (%)	42.2	53.2	0.06
Lower endoscopy (%)	53.2	72.4	<0.01
EUS (%)	49.1	52.6	0.7

Table 4.

Month	RT-PCR tested pts	Positive RT-PCR pts, n (%)
June 2020	314	2 (0.6)
July 2020	371	0 (0)
August 2020	397	10 (2.5)
September 2020	247	11 (4.5)
October 2020	281	11 (3.9)
November 2020	226	6 (2.7)
December 2020	180	12 (6.7)
January 2021	378	12 (3.2)
February 2021	146	7 (4.8)
Total	2540	71 (2.8)

difference was statistically significant ($P<0.01$). In detail for Unit 1 the reduction was 42.2%, 53.2% and 49.1% for upper GI endoscopy, lower GI endoscopy and EUS, respectively. For Unit 2 the reduction was 53.2%, 72.4% and 52.6% for upper GI endoscopy, lower GI endoscopy and EUS, respectively. No significant differences were detected in the decrease of upper GI endoscopies and EUS between the two endoscopy units. Moreover, considering EUS as part of upper GI endoscopy, there was a reduction from 2835 to 1308 procedures at Unit 1 (55.9%) and a reduction from 1937 to 806 at Unit 2 (58.4%). This difference was not statistically significant.

Finally, the decrease in lower GI endoscopies was significantly more evident in the Unit 2 compared to Unit 1 (72.4% v.s. 53.2%; $P<0.01$) (Table 3).

3. Pre-procedure real-time PCR testing

Two-thousand-five-hundred-ninety-six patients have been scheduled for pre-procedure real-time PCR testing within 48 hours before endoscopy at Unit 2. Fifty-six (2.2%) patients did not perform real-time PCR testing and scheduled endoscopy was canceled. Among the 2540 patients tested with real-time PCR, 71 were positive (2.8%) and 2469 (97.2%) negative. The prevalence of SARS-CoV2 infection at real time-PCR for every single month of the study period is reported in Table 4.

Seventy-six negative patients (3.1%) did not show up for scheduled endoscopy and therefore, 2393 patients underwent endoscopy with a negative real-time PCR.

The mean age of the 71 patients with positive real-time PCR was 57.8 ± 14.8 years and 40 were males (56.3%). Patients with negative real-time PCR had a mean age of 60.5 ± 16.3 years and 1256 were males (50.9%). No statistically significant differences were found in age and gender prevalence between patients with positive or negative real-time PCR.

Among the 71 patients who had endoscopy postponed because of positive real-time PCR, only 55 (77.5%) performed endoscopy over the following 12 months. The mean time lag between first scheduled endoscopy appointment and the endoscopic procedure was 61.7 days (range 9-294). Among these, 29 patients (52.7%) underwent lower GI endoscopy, 24 (43.6%) upper GI endoscopy, and 3 (5.5%) EUS. No clinically significant diagnoses were delayed in patients undergoing upper GI endoscopy and EUS, while in patients undergoing lower GI endoscopy a colon cancer was diagnosed after 37 days from the first scheduled endoscopy, and four advanced adenomas were diagnosed after 42, 49, 145, 153 days, respectively.

Sixteen out of the 71 patients with positive real-time PCR (22.5%) did not perform any endoscopic procedure in the following 12 months and were considered lost at follow-up.

Discussion and conclusions

SARS-CoV2 infection is having severe consequences on the general Health Systems, including endoscopic activity. The present study shows that the adoption of routinary pre-procedure real-time PCR for SARS-CoV2 in combination with symptom screening implies no clear benefits in preventing HCWs infections, compared to symptom screening alone, independently of vaccination status. Moreover, our data suggest that this strategy might induce a stronger decrease in endoscopic activity and might contribute to diagnostic delay of GI pathologies.

The novel AGA guidelines² reported 8 studies focusing on SARS-CoV2 infection among HCWs in endoscopy units, with a rate ranging from 0% to 4.0% (7,13-18). Differently from these data, the present study reports a significantly higher overall infection rate among HCWs (9/64, 14%). This discrepancy might be explained considering the relatively long period of analysis (9 months). However, only 2 out of the 9 infected HCWs (3.1%) had symptoms and none required hospitalization. Interestingly, in the Endoscopy Unit where pre-procedure real-time PCR was not in use, the overall infection rate among HCWs was lower during the study period, even though not significantly different (9% vs. 19.3%). These data support the AGA recommendation against pre-endoscopy testing for SARS-CoV2 in asymptomatic patients undergoing endoscopy. Furthermore, our study suggests that, regardless of vaccination, the risk of SARS-CoV2 infection in endoscopy HCWs does not decrease with a pre-procedure real-time PCR screening. This result might be explained considering the efficacy of personal protective equipment in protecting HCWs and the potentially marginal role of endoscopy exposure in the risk of infection of HCWs (15).

Many published studies reported a significant decrease in the number of performed upper and lower endoscopies during the SARS-CoV2 pandemic, accounting for 57%-72% and 45%-85%, respectively (19,20). In agreement with the literature, both centers included in the present study have strongly reduced endoscopic outpatient activity. However, in the Endoscopy Unit requiring pre-procedure real-time PCR (Unit 2), this decrease was significantly higher (61.9% v.s. 53.4; $P > 0.01$). This difference is not simply explainable with the exclusion of few positive asymptomatic patients. The need of pre-procedure real-time PCR makes scheduling more difficult, especially in case of replacing cancelled endoscopic procedures. Moreover, considering the implications of a positive SARS-Cov2 testing in everyday life, asymptomatic patients might avoid this practice, postponing endoscopic investigation. Interestingly, both Units had a higher decrease in lower GI endoscopies compared to upper GI endoscopies which is not clearly explainable. A greater decrease in lower GI endoscopies compared to upper GI endoscopies was also reported in a study published by Kahn and colleagues (19) on a retrospective cohort from US between March 15th and

July 15th 2020. The authors reported a decrease in upper endoscopies, colonoscopies and EUS of 71.8%, 84.7%, and 73.1%, respectively. Differently, authors from the Netherlands²⁰ reported a greater decrease in upper GI endoscopies (57%) compared to colonoscopies (45%) during the period between March 15th and June 15th 2020.

A possible explanation of the prevalent decrease in colonoscopies compared to upper GI endoscopies reported in our study might be related to the indication for endoscopy. A significant proportion of colonoscopies are performed for preventive or follow-up reasons in asymptomatic patients, while upper GI endoscopy is frequently performed to investigate specific symptoms. We might assume that asymptomatic patients might consider postponing endoscopy more likely than symptomatic patients.

Considering the well described phenomenon of reduction in cancer diagnosis during SARS-CoV2 pandemic,² any factor associated to a further decrease in endoscopic activity should be avoided. Moreover, a delayed cancer diagnosis in patients who postponed endoscopy for a positive pre-endoscopy real-time PCR might lead to significant clinical and legal consequences.

Possible theoretical advantages might be related to pre-endoscopy real-time PCR testing, such as identifying asymptomatic SARS-CoV2 infections needing isolation and monitoring real-life infection prevalence. Patients undergoing real-time PCR in general health care setting are generally symptomatic or had close contact with positive patients suggesting a possibly higher infection prevalence compared to the general population. Therefore, patients scheduled for endoscopy might represent a better indicator of the real infection prevalence in the general population.

However, our data fully agree with the AGA guidelines, confirming no advantages and underlying possible substantial disadvantages of pre-endoscopy real-time PCR in outpatients setting. Moreover, the analysis of a pre-vaccination period strongly supports the efficacy of PPE in preventing SARS-CoV-2 infection in endoscopy HCWs. Considering the additional undoubted advantage of vaccination there are no clinical advantages in performing real-time PCR testing before outpatient endoscopy. Based on these results, the use of additional PPE for endoscopy procedures in SARS-CoV2 positive patients might be also reconsidered and should be further investigated.

The present study has several strengths. First, it represents, at our knowledge, the first study comparing pre-procedure testing in combination with symptom screening vs symptom screening alone in endoscopy units. Moreover, it includes a fair number of endoscopic procedures, involving two similar high-volume endoscopic units working in the same geographical area, avoiding bias related to different SARS-CoV2 prevalence. Finally, the analysis includes a long (9 months) pre-vaccination period, avoiding bias related to different

immunological statuses depending from the time elapsed since the last vaccination.

However, some limitations need to be addressed. Besides the retrospective design, counterbalanced by a prospective data collection, a major bias is represented by the small number of included HCWs. The decision not to involve other endoscopy units in order to enlarge the study populations was taken with the aim to avoid potential relevant bias related to SARS-CoV2 prevalence of different geographical areas.

In conclusion, our data suggest that pre-endoscopy testing for SARS-Cov2 does not provide any benefit in terms of HCWs infection and can be actually associated to a greater decrease in endoscopic activity and potentially to diagnostic delay.

Authors contribution

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Final approval: all the authors

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