

# Analysis of the effects of the first and second/third waves of the COVID-19 pandemic on an Interdisciplinary Endoscopy Unit in a German 'hotspot' area: a single-center experience

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## Abstract

**Background:** Since December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed a pandemic threat to global health. We are now in the fourth wave of this pandemic. As the pandemic developed, the requirements and therapeutic endoscopic procedures for SARS-CoV-2-positive patients underwent changes.

**Methods:** Analysis of implications for an endoscopy unit during the first and second/third waves of the COVID-19 pandemic with a focus on COVID-19-related process changing. Addressed are number of SARS-CoV-2-positive patients and endoscopic examinations performed in patients who tested positive for SARS-CoV-2 during the various waves, adherence to scheduled examinations, rotation of staff to COVID-dedicated structures and, finally, impact of vaccination on infection rate among endoscopic staff.

**Results:** During the first wave, 10 SARS-CoV-2-positive in-house patients underwent a total of 22 gastrointestinal (GI) endoscopic procedures. During the second and third waves, 59 GI endoscopies were performed in 38 patients. While in the first wave, GI bleeding was the main indication for endoscopy (82%), in the second and third waves the main indication for endoscopy was endoscopic insertion of deep feeding tubes (78%;  $p < 0.001$ ). During the first wave, 5 (17%) of 29 Interdisciplinary Endoscopy Unit (IEU) staff members were moved to designated COVID wards, which was not necessary during the following waves. Lack of protective clothing was critical during the first wave, but not in the later waves. Screening tests for patients and staff were widely available after the first wave, and IEU staff was vaccinated during the second wave.

**Conclusion:** Strategies to ensure safe endoscopies with respect to preventing transmission of SARS-CoV-2 from patients to staff were effective. Organizational adjustments allowed the routine program to continue unaffected. Indications for GI endoscopies changed over time: during the first wave, GI endoscopies were performed for life-threatening indications, whereas later supportive procedures were the main indication.

**Keywords:** change in indication, COVID-19, impact of vaccination, implications for interdisciplinary endoscopy, risk of infection

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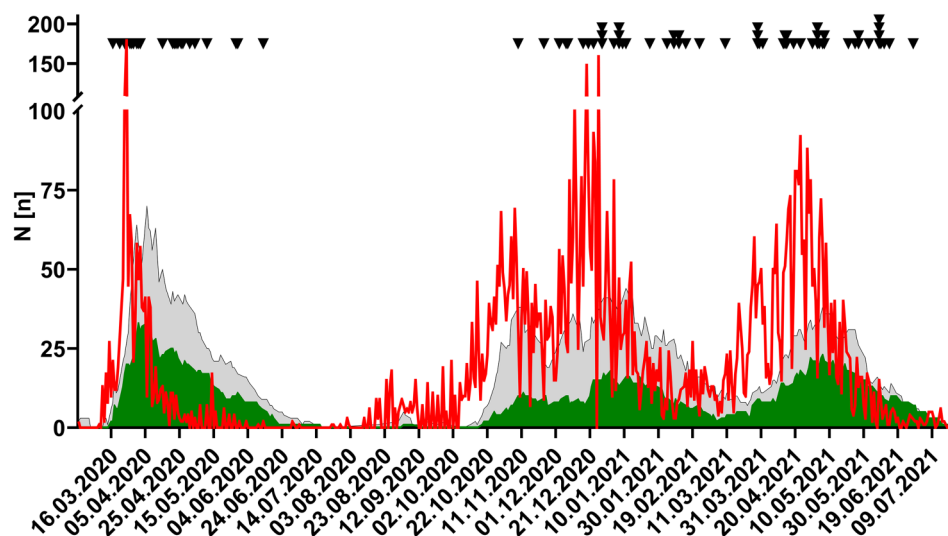
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**Figure 1.** Timeline for development of the 2020/2021 SARS-CoV-2 pandemic in Tübingen District, Baden-Württemberg, Germany. The peaks of the three waves of SARS-CoV-2 are clearly depicted. Red line: Daily incidence of PCR-positive SARS-CoV-2 infections in Tübingen District. Gray area: Hospitalized SARS-CoV-2 patients. Green area: SARS-CoV-2 patients on ICU. Black arrowheads: Endoscopic intervention in SARS-CoV-2-positive patients. ICU, intensive care unit.

## Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has changed our world profoundly.<sup>1,2</sup> This pandemic, which emerged in China in late 2019, has affected societies and health systems worldwide. SARS-CoV-2 has posed a severe test for most countries.<sup>3-5</sup> Many people, over 4 million so far, have died from or with SARS-CoV-2, and it is not yet clear how many will suffer from secondary diseases ('long COVID syndrome'). Countries in the Far East were often prepared for such a pandemic, having previously dealt with SARS-CoV-1 and avian influenza (H5N1).<sup>6</sup> Most Western countries have struggled to adapt to the pandemic.<sup>7</sup>

In Central Europe, the first wave peaked in April 2020 and ended in June 2020. During that period, healthcare systems came to the brink of collapse or even beyond.<sup>8</sup> In addition, healthcare professionals (HCP) had to adapt to the new disease and develop algorithms for diagnosis, risk stratification, and treatment of SARS-CoV-2.<sup>9-11</sup> At the same time, shortages of protective equipment had to be overcome.<sup>12,13</sup>

In the field of gastroenterology, especially endoscopy, the focus is on monitoring, diagnosing, and

treating patients with chronic or acute gastrointestinal (GI) diseases. These procedures should be safe for SARS-CoV-2-positive and SARS-CoV-2-negative patients. The endoscopy staff should be exposed to as little risk as possible. Regarding diagnosis, endoscopy is one of the most affected procedures and the impact of the decrease in procedures is yet to be determined.<sup>14,15</sup>

We analyzed what these adjustments meant for an Interdisciplinary Endoscopy Unit (IEU) of a tertiary center in a SARS-CoV-2 hotspot area that had the second highest 7-day incidence in Germany on 31 March 2020 (205.9/100,000, [www.rki.de](http://www.rki.de); the peak *daily* incidence in Tübingen was 179/100,000 on 25 March 2020), exactly at the peak of the first wave in Germany<sup>16</sup> (see Figure 1).

Now, on the eve of the fourth wave of SARS-CoV-2 in Central Europe, we look back and critically analyze how our IEU adapted to the pandemic; we do this by comparing the first wave with the second/third waves. We analyzed the impact of SARS-CoV-2 (1) on processes in the IEU, (2) on IEU staff, (3) and subsequently conducted a prospective analysis of GI endoscopic interventions in patients with confirmed or suspected SARS-CoV-2 infection.

**Table 1.** Patient characteristics, endoscopic specifications, and outcome of COVID-19 patients in the first SARS-CoV-2 wave in early 2020 and the second/third SARS-CoV-2 waves from autumn 2020 to summer 2021, who underwent GI endoscopic treatment.

		Total	First wave	Second/third wave	<i>p</i>
Number of patients	<i>N</i>	48	10 <sup>a</sup>	38	–
Duration of wave (weeks)		62	19	43	–
Age (years)	Median	59	61.5	58	0.194
	IQR	53.5–65	56.75–75.5	52–64	
	Range	27–90	50–83	27–90	
Sex (male)	<i>n</i> (%)	36 (75%)	7 (70%)	29 (76%)	0.685
APACHE score <sup>b</sup>	Median	22	21	22.5	0.23
	IQR	18–26	16–24.75	18–26	
	Range	14–31	14–25	14–31	
Invasive ventilation	<i>n</i> (%)	43 (89.6%)	6 (60%)	37 (97.4%)	<0.001
ECMO	<i>n</i> (%)	28 (58.3%)	5 (50%)	23 (60.5%)	0.552
Endoscopies <sup>c</sup>	<i>N</i>	81	22	59	–
Endoscopies per patient <sup>c</sup>	Mean	1.7	2.2	1.6	0.263
	Range	1–5	1–5	1–4	
Endoscopies per week	Mean	1.3	1.2	1.97	0.806
	Range	0–7	0–5	0–7	
Indications for endoscopy	GI bleeding	29 (36%)	18 (82%)	11 (19%)	<0.001
	Nourishment	48 (59%)	2 (9%)	46 (78%)	
	Other	4 (5%)	2 (9%)	2 (3%)	
Site of endoscopy	ICU	77 (95%)	19 (86%)	58 (98%)	0.28
	NP room	2 (2%)	1 (5%)	1 (2%)	
	X-ray room	2 (2%)	2 (9%)	0	
Outcome (death)	<i>n</i> (%)	27 (56%)	5 (50%) <sup>a</sup>	22 (58%)	0.717

APACHE, Acute Physiology and Chronic Health Evaluation; COVID-19, coronavirus disease; ECMO, extracorporeal membrane oxygenation; GI, gastrointestinal; ICU, intensive care unit; IQR, interquartile range; NP, negative pressure; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

<sup>a</sup>Of the 10 patients, one was not infected with SARS-CoV-2, but was treated as if infected since this was a contact person of a SARS-CoV-2 PCR-positive patient at our center at the very beginning of the pandemic. Outcome without that patient: dead 5/9, 56%.

<sup>b</sup>Data for calculation of APACHE score were available for 37/48 patients.

<sup>c</sup>When several examinations were performed simultaneously (e.g. combined gastroscopy and colonoscopy), these were counted as one examination.

## Materials and methods

### Study design

This is a combined study including a prospective analysis of endoscopic interventions in

SARS-CoV-2-positive patients during the first and second/third waves of the COVID-19 pandemic in Germany as well as a descriptive part about logistic changes and the impact of COVID-19 on the daily routine in an Interdisciplinary

Endoscopic Unit (IEU). The patient selection was selective. All SARS-CoV-2-positive patients with GI endoscopic procedures were included.

Results are presented in Table 1 and Figures 1–3: (1) comparison of demographic patient parameters of the first and the second/third waves of SARS-CoV-2 at our center, (2) SARS-CoV-2 pandemic-related restructuring of processes at the IEU, (3) SARS-CoV-2 pandemic-related impact on the IEU staff, and (4) analysis of endoscopic interventions needed in patients with confirmed or suspected SARS-CoV-2 infection.

The local ethics committee of Tübingen University Hospital, Germany, approved this study (AZ: 242/2020BO2) and it is registered with ClinicalTrials.gov (NCT04423003). Investigation period was March 2020 to July 2021. Informed consent for endoscopy was obtained from each participant or from their legal guardian. Ethics Approval and Consent to Participate together with informed consent was obtained from all participants. In addition, we have de-identified the details such that the identity of the patients may not be ascertained in any way.

The reporting of this study conforms to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement: guidelines for reporting observational studies (see supplementary material 1).

#### Database

Data are available in SPSS v. 24.0.0.1 (IBM, Armonk, NY, USA) and were presented as mean  $\pm$  SD.

## Results

### *Demographic parameters during the first and the second/third waves of SARS-CoV-2*

During the first wave (26 February to 30 June 2020), 249 SARS-Cov-2 polymerase chain reaction (PCR)-positive patients needed hospitalization, 88 (35%) of whom were treated at the intensive care unit (ICU). Forty-one patients died due to or with a SARS-CoV-2 infection during that period (16.4% of all inpatients). From the end of the first wave to the end of the third wave (from 1 July 2020 to 30 June 2021), 726 SARS-Cov-2 PCR-positive patients were treated

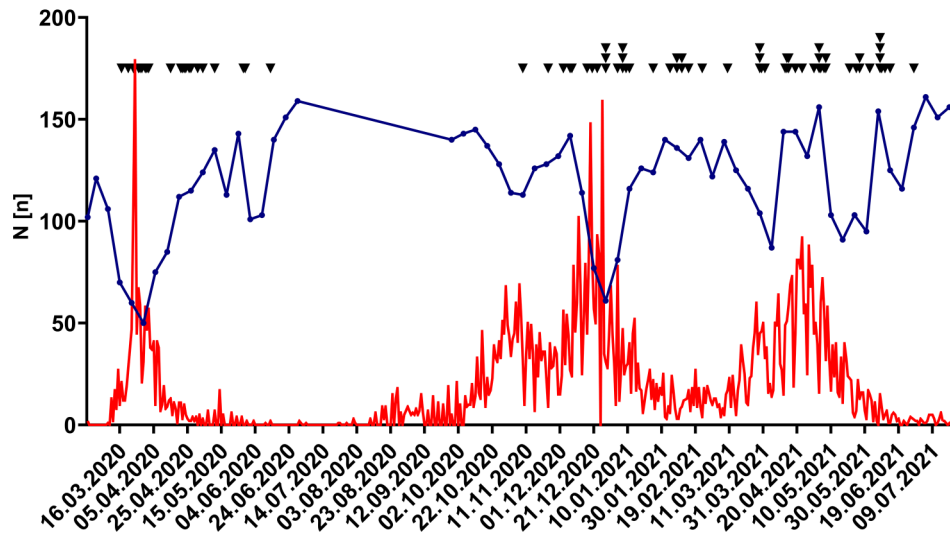
as inpatients, 160 (22%) of whom required ICU support. During that period (second/third waves), 88 patients died due to or with a SARS-CoV-2 infection (12% of all inpatients).

### *SARS-CoV-2-pandemic-related process changes at the IEU*

*Cancellation of interventions.* Because of the still limited knowledge about the new virus and the lack of alternatives, at the beginning of the first wave, a decision was made to limit patient access to the IEU. This resulted in less than 50% endoscopies of pre-pandemic access (namely 46% of the weekly average, see Figure 2). The decision as to which formally elective procedures could still be performed despite the SARS-CoV-2 lockdown was made by an expert board. They included preventive measures such as ligation therapy of esophageal varices after variceal bleeding, or diagnosis of suspected cancer.<sup>16</sup> During the second wave, the percentage of GI endoscopies decreased to 43%. The peak of the second wave coincided with the 2020 Christmas holidays. This shortened the work week by 2 days and may have affected the number of endoscopies performed at that time. In addition, the reduced staff on duty over the holidays meant only few elective procedures were scheduled. During the third wave, the number of GI endoscopies remained stable (93%). Because SARS-CoV-2 antigen testing was available in sufficient quality and quantity from September 2020, patients could then be tested for SARS-CoV-2 prior to hospital admission (see Figure 3 for a flow chart). For inpatients, an in-house PCR test was compulsory. In addition, vaccination against SARS-CoV-2 was offered to medical staff and certain patient groups starting in January 2021. With this strategy, the number of GI endoscopies did not significantly decrease, at least not during the third wave of SARS-CoV-2. Despite these safety precautions, to our knowledge, two in-house patients who tested negative were later diagnosed as SARS-CoV-2-positive following an endoscopy in our unit, but without any infection of staff members.

### *Separation of patients at risk and procedural measures.*

During the first wave of SARS-CoV-2, various measures were taken to isolate known infected patients from staff and uninfected patients. Patients who tested positive were isolated in an infectious disease ward and later in dedicated additional SARS-CoV-2 wards. Accordingly, a dedicated SARS-CoV-2 ICU was



**Figure 2.** Weekly numbers of gastrointestinal endoscopies performed at the Interdisciplinary Endoscopy Unit of Tübingen University Hospital. Two dips in the line (blue line) correlate with the peaks of the first and the second SARS-CoV-2 waves in Tübingen (red line). During the third wave, the number of gastrointestinal endoscopies was not affected. Each arrowhead indicates a gastrointestinal endoscopy in a SARS-CoV-2 positive patient.

established. This resulted in an overall reduction in workload and patient turnover in other units.<sup>16</sup>

Specifically, a dedicated endoscopic tower was provided for endoscopy in the SARS-CoV-2 area to avoid cross-contamination. For SARS-CoV-2-positive patients not on the ICU, a negative pressure room with laminar air flow was established in compliance with ESGE (European Society of Gastrointestinal Endoscopy) guidelines, but was used only twice.

Patients with a positive SARS-CoV-2 PCR test, who repeatedly had a cycle threshold value greater than 30 without symptoms, were declared noninfectious and treated in the regular IEU.<sup>17–19</sup> In the first wave, 86% of endoscopic procedures were performed in the ICU, whereas in the second/third waves, 98% of endoscopic procedures on SARS-CoV-2 positive patients were performed in the ICU ( $p=0.28$ ).

#### *SARS-CoV-2 pandemic-related impact on the IEU staff*

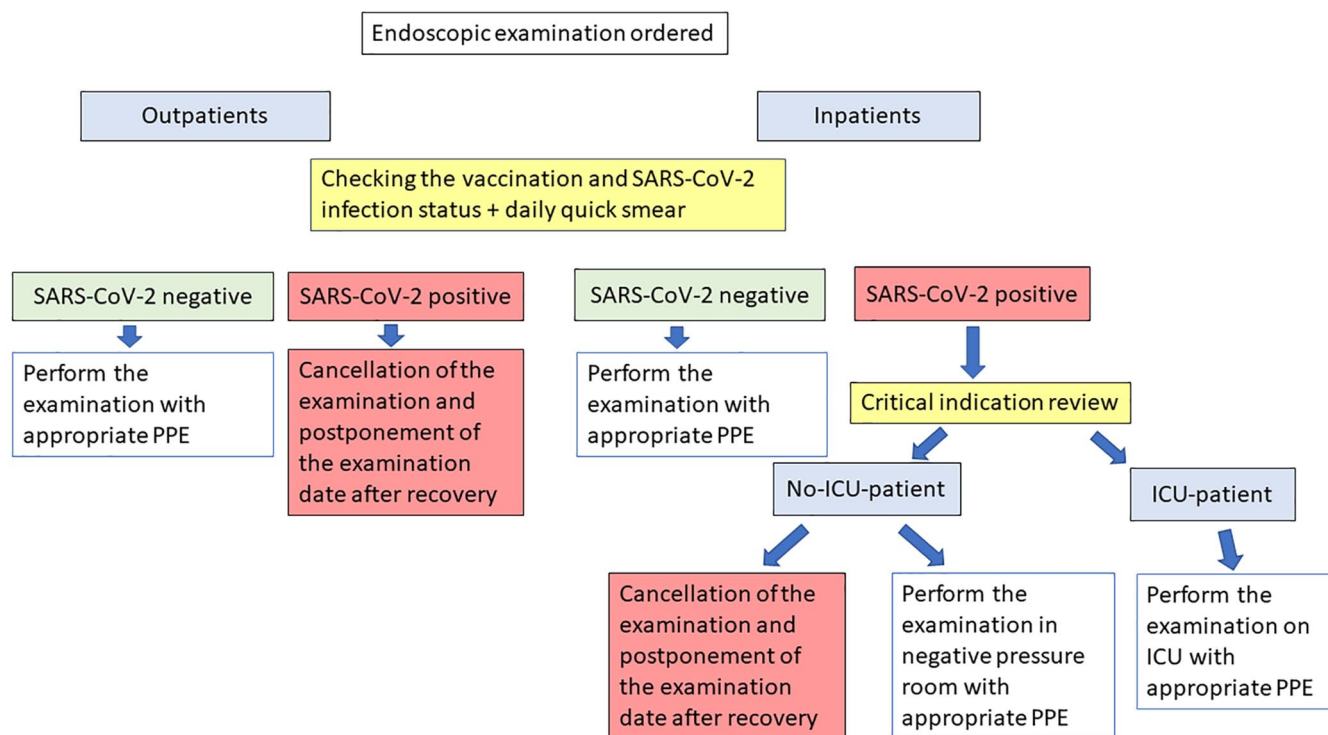
*Rotation of medical staff from the IEU to COVID-19 wards.* During the first wave, 2 (18%) of 11 physicians and 3 (17%) of 18 nurses at the IEU were redeployed to COVID-19 units.<sup>16</sup> During the

second/third waves, no staff rotation was needed. This was because the number of hospitalizations during the second/third waves did not exceed the capacities of the new COVID-19 facilities.

*SARS-CoV-2 infections, quarantine, SARS-CoV-2 point-prevalence study of IEU staff.* Two (18%) of 11 physicians who tested positive for SARS-CoV-2 during the first wave had to go into quarantine and two additional physicians were relieved of duty because of pregnancy. Later during the first wave, a point-prevalence analysis showed that no one on the staff was PCR-positive for SARS-CoV-2. During the second/third waves rapid antigen tests were widely available and therefore, starting in September 2020, IEU staff members were tested weekly with an antigen swab. During the second wave, one (6%) nurse out of 18 tested positive for SARS-CoV-2. During the third wave, no further infections of IEU staff were detected.

*Supply of protective clothing.* A critical problem during the first wave of SARS-CoV-2 was the lack of protective clothing, mainly the shortage of protective masks and splash guards. However, from early summer 2020, the supply of protective clothing was no longer a problem in the treatment of SARS-CoV-2 patients.





**Figure 3.** Flowchart depicting the decision-making processes for patient access to the Interdisciplinary Endoscopy Unit of Tübingen University Hospital since the third wave of SARS-CoV-2. ICU, intensive care unit; PPE, personal protective equipment.

**Vaccination.** Following approval of the SARS-CoV-2 vaccines, all employees of Tübingen University Hospital who could potentially come into contact with SARS-CoV-2 were able to be voluntarily vaccinated from 3 January 2021. The vaccination was performed by a specially established in-house infrastructure. All IEU staff members were vaccinated by the end of January, except those who had already had a PCR-confirmed SARS-CoV-2 infection. Those persons later received a booster vaccination. Some of the staff have so far received a third vaccination, which was undertaken at their personal initiative in public vaccination centers. Vaccination at Tübingen University Hospital was performed with the Biontech/Pfizer mRNA-vaccine *COMIRNATY*. According to new legislation, all staff of the IEU is now (March 2022) triple-vaccinated.

#### *Endoscopic interventions in patients with confirmed or suspected SARS-CoV-2 infection*

We analyzed GI endoscopic interventions between 1 March and 30 June 2020 (first wave of the pandemic) in patients with confirmed or

suspected SARS-CoV-2 infection. For the second and third waves, we analyzed the core wave period between 1 October 2020 and 30 June 2021 (see Table 1 for details). During the first wave, 22 GI endoscopic procedures (mean per patient 2.2) were performed in 10 SARS-CoV-2-positive patients (m:f = 70%:30%, median age 61.5). During the longer period of the second/third waves, 59 GI endoscopic procedures were performed in 38 patients (m:f = 76%:24%;  $p = 0.685$ , median age 58,  $p = 0.194$ , mean per patient 1.6,  $p = 0.263$ ). This meant 1.2 endoscopies per week in the first wave and 1.97 endoscopies per week in the second/third waves ( $p = 0.806$ ). In both observation periods, the median APACHE (Acute Physiology and Chronic Health Evaluation) III score<sup>20</sup> at the time of the first endoscopy was similar (21 versus 22.5,  $p = 0.23$ ), implying a projected mortality of 40% at the time of the first endoscopy for both groups. However, an APACHE score could not be calculated in a subset of patients (9 of 48). Most of these patients were not on the ICU, so the median APACHE score could probably have been set higher than it actually was. In the second/third waves, most patients (37

of 38, 97.4%) were invasively ventilated at the time of the first endoscopy, whereas in the first wave only 6 (60%,  $p < 0.001$ ) of 10 patients were invasively ventilated. In both groups, slightly more than half of the patients were on extracorporeal membrane oxygenation (ECMO) at the time of the first endoscopy (first wave 6 of 10, 60%; second/third waves 23 of 38, 60.5%;  $p = 0.552$ ). Considering the larger proportion of patients without a calculable APACHE score and the smaller number of patients with invasive ventilation and ECMO in the first wave, second/third wave patients were most likely more severely affected than were first wave patients.

A significant difference between the two groups was the indication for endoscopy: while in the first wave endoscopy was indicated because of life-threatening GI bleeding (18 of 22, 82%), in the second/third waves endoscopy was performed for placement of deep feeding tubes (46 of 59, 78%;  $p < 0.001$ ). Consistent with the severe disease of almost all patients in both waves, the main endoscopy site was the ICU (first wave 19 of 22, 86%; second/third waves 58 of 59, 98%;  $p = 0.28$ ).

## Discussion

In this study, we prospectively analyzed the impact of the SARS-CoV-2 pandemic on the IEU of a tertiary center in southwestern Germany. Furthermore, restructuring processes in response to the pandemic was noticed, as well as the impact on IEU staff and indication for endoscopic GI interventions in COVID-19 patients. In addition, to our knowledge for the first time, we analyzed differences between the first wave (for Tübingen, 26 February–30 June 2020)<sup>16</sup> and the combined second/third waves (1 July 2020–30 June 2021, with the core period from 1 October 2020–30 June 2021).

Regarding the overall impact of COVID-19 on our institution, the rate of patients with ICU treatment was higher in the first wave than in the second/third waves (35% *versus* 22%), as was mortality (16.4% *versus* 12%). Reasons for the smaller proportions of patients in each of the two groups in the second/third waves could be a better understanding of the disease and specific treatment (steroids, antibodies) and, especially in the third wave, the effect of vaccination, which may have attenuated the course of the disease in vaccinated patients. In another southwestern German tertiary center, in the first wave 33% of in-house

patients needed ICU treatment and the projected mortality was 16–24%,<sup>21</sup> thus nearly identical with the results for the first wave at our center.

As for the IEU restructuring processes, GI endoscopies were reduced to 46% in general during the first wave, whereas no significant impact on the weekly average of GI endoscopies was seen during the third wave. This was most likely due to the widespread availability of rapid antigen and PCR testing for SARS-CoV-2 at that time, which was mandatory in patients undergoing elective and emergency GI endoscopies. In addition, during the third wave, an effect of the now widely available vaccination against SARS-CoV-2 may have already been felt. However, at the peak of the second wave, GI endoscopic activity was reduced to 43%, which was certainly a combined effect of the ‘lockdown’ measures and the coincidence of the wave peak with the 2020 Christmas holidays resulting in fewer working days. During the first wave, in other centers in Germany and Northern Italy, endoscopic programs had to be reduced to 1–60%.<sup>22,23</sup>

In the first wave of the pandemic, part of the IEU staff (5 of 29; 17%) was reassigned to the newly created COVID ICU, which was no longer necessary in the following waves, as resilient structures for the treatment of COVID-19 patients had been created and the second/third waves did not put as much strain on the organization of Tübingen University Hospital as did the first wave. In Northern Italy, 65.9% of centers redeployed physicians, and 75.6% of centers redeployed nurses to other departments.<sup>23</sup>

Concerning the impact of SARS-CoV-2 on IEU staff, a total of 3 (10%) of 29 staff were infected during the pandemic, 2 with no or only mild symptoms and 1 with flu-like symptoms. However, none of them contracted the virus on the job. Thus, infection prevention measures, which changed during the pandemic, were seen to be effective, at least for IEU staff. There were differences in protective measures between waves: during the first wave when protective clothing was lacking and limited means were available for rapid identification of infected individuals (no antigen swabs, only PCR testing in limited numbers), reducing exposure to elective patients, along with the partially improvised protective clothing, was the main feature of transmission prevention. During the second wave, the

expansion of rapid testing capacity inside and outside the hospital and the ample supply of protective clothing protected staff in a standardized and safe manner, although the number of GI endoscopies decreased in the same degree as during the first wave, likely due to the coincidence of the main wave with the 2020 Christmas holidays. However, during the third wave, in addition to the second wave measures, IEU staff were able to be actively protected by vaccination. Thus, there was no longer a decline in endoscopies during the third wave.

Importantly, no transmission of SARS-CoV-2 from patients to our staff was observed during any wave, so our protective measures appear to have been effective. Accordingly, a multicenter study confirmed our local findings showing a minimal infection rate in a lockdown situation with provision of personal protective measures.<sup>24,25</sup> During the pandemic, we were able to comply with ESGE recommendations<sup>26</sup> to establish a negative pressure room with laminar air flow for endoscopy. However, during the entire pandemic, it was actually used only twice, as we had an internal agreement permitting us to perform endoscopies in positive patients at the ICU, if possible only with an emergency indication. Therefore, in our opinion, the provision of a negative pressure room is not an absolute requirement for COVID-19 patients, because elective endoscopic procedures can generally be postponed until the patient recovers from COVID-19.<sup>27</sup>

We analyzed endoscopic procedures in COVID-19 patients during the first wave and, collectively, the second/third waves. We found similar patient characteristics in both groups in terms of age, sex distribution, and APACHE score at the time of the first endoscopy. However, in the first wave, a number of patients were not ventilated at the time of first endoscopy, resulting in a significant difference in both groups. One patient had GI bleeding and required noninvasive ventilation; another was a contact person to a SARS-CoV-2-positive patient and was therefore treated as a positive patient. This was our usual approach at the very beginning of the pandemic, when contact persons were also isolated for an extended period if they had to stay at the hospital for medical reasons. In addition, we observed a marked shift from mainly life-threatening indications (GI bleeding) during the first wave to supportive indications (insertion of feeding tube) in the second/third waves.

The respiratory impairment of COVID-19 patients often makes ECMO necessary. The autopsies of the first COVID-19 patients revealed microthrombi in central vessels of the lung, heart, brain, and upper abdominal organs. To counteract this, anticoagulation was strongly escalated in COVID-19 patients during the first wave. In the second/third waves, anticoagulant therapy was more moderately adjusted. Zellmer *et al.* examined the incidence of GI bleeding in COVID-19 patients and reported that there is no difference in incidence compared to non-COVID-19 patients in similar settings or in other clinical scenarios. During the critical stage of disease, being on a therapeutic dose of anticoagulation was associated with a significant increase in the risk for GI bleeding.<sup>28</sup>

In conclusion, strategies at Tübingen University Hospital and its IEU were effective in ensuring safe endoscopies with regard to preventing transmission of SARS-CoV-2 from patients to staff and had the positive effect that the routine IEU program was not massively affected by the ongoing pandemic. Indications for GI endoscopies changed over time: during the first wave, GI endoscopies were performed for life-threatening indications, while supportive procedures were later the main indications.

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### Author contributions

**Dörte Wichmann:** Conceptualization; Data curation; Formal analysis; Investigation; Project administration; Validation; Writing – original draft; Writing – review & editing.

**Ulrike Schempf:** Data curation; Investigation; Writing – review & editing.

**Siri Göpel:** Data curation; Formal analysis; Writing – review & editing.

**Dietmar Stüker:** Formal analysis; Writing – review & editing.

**Stefano Fusco:** Data curation; Writing – review & editing.

**Alfred Königsrainer:** Conceptualization; Formal analysis; Supervision; Validation; Writing – review & editing.

**Nisar P. Malek:** Conceptualization; Supervision; Validation; Writing – original draft; Writing – review & editing.



**Christoph R. Werner:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Validation; Visualization; Writing – original draft; Writing – review & editing.

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### Supplemental material

Supplemental material for this article is available online.

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