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Marco Raffaelli, MD\*, Carmela De Crea, MD, Luca Sessa, MD,  
Rocco Bellantone, MD

UOC Chirurgia Endocrina e Metabolica, Fondazione Policlinico  
Universitario Agostino Gemelli IRCCS, Rome, Italy

Dipartimento Universitario di Medicina e Chirurgia Traslationale,  
Università Cattolica del Sacro Cuore, Rome, Italy

\* Corresponding author.

E-mail address: [marco.raffaelli@unicatt.it](mailto:marco.raffaelli@unicatt.it) (M. Raffaelli);

Twitter: @twitter handle

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### Peritoneal swab test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients in abdominal surgery: Is it a reliable practice?



We read with great interest the article by Seeliger et al<sup>1</sup> in which the authors determined the possible detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in peritoneal fluid in a series of coronavirus disease 2019 (COVID-19)–symptomatic patients undergoing emergency abdominal surgery. In their study, intraperitoneal SARS-CoV-2 infection was not detectable on reverse transcriptase–polymerase chain reaction in any of these patients. We would like to raise some interesting points. The safety of laparoscopic surgery in SARS-CoV-2 patients still remains unclear. The possible contamination of peritoneal fluid by SARS-CoV-2 is a current matter of debate in recent COVID-19 scientific literature. In 1996, Des Coteaux et al<sup>2</sup> demonstrated the presence of breathable aerosols and cell-size fragments in the cautery smoke produced during laparoscopic procedures. About 5% of the volume of aerosol contains small particles, which may pass through the usual surgical mask or may be inoculated into the ocular conjunctiva. However, the size of the aerosolized particles depends on the type of energy used. Aerosolization of blood-borne viruses like hepatitis B virus, HIV, and human papillomavirus has been previously detected in surgical smokes during laparoscopy.<sup>3</sup> Due to COVID-19 pandemic spread, surgical societies focused their attention on the safety of the health care workers who are directly involved in the clinical management of SARS-CoV-2 positive patients.

To date, surgical consensus guidelines<sup>4</sup> (eg, Royal College of Surgeons, European Association of Endoscopic Surgery, Society of American Gastrointestinal and Endoscopic Surgeons) recommend caution in the use of laparoscopy for the theoretical possibility of viral transmission from aerosolization of tissue and peritoneal fluid during surgery. The presence of SARS-CoV-2 in peritoneal fluid has been demonstrated,<sup>5,6</sup> although several reports suggest that it is often undetected.

Three important issues need to be addressed:

1. Peritoneal membranes have maximum pore diameter of 20 to 40 nm, whereas SARS-CoV-2 virion diameter is approximately

50 to 200 nm.<sup>7</sup> Therefore, viral translocation across the peritoneal membrane barrier may theoretically occur only in case of damaged peritoneal permeability or inflammation.

2. The cell membrane protein angiotensin-converting enzyme-2 is key for receptor-mediated cell entry of SARS-CoV-2. It is expressed in pneumocytes (type II alveolar cells) as well as in the gastrointestinal tract, in particular in ileal and colonic enterocytes, which may represent a theoretical route of peritoneal fluid contamination during both open and laparoscopic surgery.
3. Currently, the laboratory method for the diagnosis of SARS-CoV-2 is only certified as qualitative, and therefore, the result of molecular swab is either negative or positive. However, the chemo-physical process required is much more complex and may lead to uncertain results. In fact, the outcome of a molecular swab does not depend only on the exceeding of a threshold value but also on the extent of such surpass. Furthermore, a weak positivity/negativity (ie, a value close to the cutoff) may depend on factors unrelated to the real viral load, such as the method of sampling, its storage, transport, etc. This could explain why patients with “low viral load” have nasopharyngeal swabs with discordant results with each other and with other body fluids. Finally, as regards swabs performed on body fluids other than the oral-pharyngeal ones, even if the method is not prohibited, it is currently not certified.

In a recent article,<sup>8</sup> we also suggested the possibility that the presence of SARS-CoV-2 in the peritoneum may depend on the disease stage. The possible correlation between higher viral loads and consequently greater viral burden in the peritoneal cavity in symptomatic patients has not been clarified yet and needs further investigation.

To date, the scientific data regarding the possibility of contagion by laparoscopic aerosolization of the virus is scant. The impact of favoring open over minimally invasive techniques could be a health burden due to prolonged duration of hospitalization and higher rate of postoperative complications, precluding the gold standard approach (ie, minimally invasive) for many patients. Certainly, health care workers must be provided with adequate personal protective equipment, and several precautions are recommended in the face of any uncertainty. We really need multicenter studies focusing on the sampling of peritoneal fluid in SARS-CoV-2 patients in order to assess the real prevalence of RNA virus, the validity of abdominal swab test, and to clarify the intraoperative risk of contagion.

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### Conflict of interest/Disclosure

None of the authors have any financial and personal relationships with other people or organizations that could potentially and inappropriately influence (bias) our work and conclusions.

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Nicolò Fabbri, MD\*, Antonio Pesce, MD, PhD, Carlo  
Vittorio Feo, MD, FACS  
Department of Surgery, Delta Hospital, Azienda USL Ferrara,  
University of Ferrara, Italy

Stefano Pizzicotti, MD  
Laboratory Division of the S Anna Hospital, University of Ferrara, Italy  
Twitter: @stefanopizzico1

\* Corresponding author.

E-mail address: [n.fabbri@ausl.fe.it](mailto:n.fabbri@ausl.fe.it) (N. Fabbri);  
Twitter: @NicolFabbri9, @antonio55428390, @Carlo\_V\_Feo

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## Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in peritoneal fluid of coronavirus disease 2019 (COVID-19) patients—Prevalence and significance



To the Editor:

We read the manuscript entitled Peritoneal swab test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients in abdominal surgery: Is it a reliable practice?<sup>1</sup> with great interest.

The authors suggest that intraperitoneal presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might remain undetected. In our study,<sup>2</sup> peritoneal fluid was sampled in syringes at the procedural beginning and/or end and analyzed in the virology laboratory on site. We expected to enable detection of intraperitoneal viral RNA via reverse transcriptase–polymerase chain reaction (RT-PCR). Our findings are in line with the majority of literature data reporting its absence in intraperitoneal fluid. In a series of 10 peritoneal dialysis (PD) patients, quantitative RT-PCR tests and additional analyses performed on PD effluent demonstrated absence of infective viral particles along with undetectable viral RNA.<sup>3</sup>

Surgery carries a high risk of morbidity and mortality, and only emergency procedures should be performed during acute coronavirus disease 2019 (COVID-19) infections. Consequently, patients amenable to analysis of intraperitoneal SARS-CoV-2 presence are rare. Intraperitoneal viral RNA detection was reported in 4 COVID-19 patients only. Intraperitoneal swab testing,<sup>4,5</sup> intraoperative fluid sampling,<sup>6</sup> and PD effluent<sup>7</sup> enabled SARS-CoV-2 RNA detection by RT-PCR. The PD effluent remained SARS-CoV-2 positive, associated with peritoneal membrane malfunction (PD failure).<sup>7</sup> Viral peritoneal cavity contamination could indeed be owing to increased peritoneal permeability during serositis or transmural bowel inflammation,

representing an advanced COVID-19 stage. We cannot yet say whether high pathogenicity results from specific virus strains, mutations, host immune, or circulatory reactions. The detection of intraperitoneal SARS-CoV-2 RNA should lead to sequencing studies, in order to gain insight on whether specific strains or mutations resulted in a virulence involving a breach of the peritoneal barrier.

While research in COVID-19 is ongoing, comparison with feline coronavirus provides additional insight. In case of inflammation, feline coronavirus can leak from the bloodstream into effusions, entailing positive intraperitoneal testing.<sup>8</sup> Similarly, to feline infectious peritonitis (FIP), the infection of macrophages could favor disease progression and explain dysregulated immune responses in COVID-19.<sup>9</sup> Antiviral drugs used in FIP are strong COVID-19 treatment candidates.

It remains unclear whether viral RNA detection is equivalent to presence of contagious virus.<sup>7</sup> The majority of articles on intraperitoneal coronavirus detection concern FIP, where RT-PCR performed on effusions has a high specificity, and a RT-PCR assay was developed to identify actively replicating virus by detecting its mRNA.<sup>8</sup>

Systematic transdisciplinary sampling in nephrological/surgical/gynecologic and autopsy settings is needed to assess the overall viral prevalence in peritoneal fluid and to discriminate between infectious material versus shedding of noninfectious viral particles. Cross-sectional data in the COVID-19 patient population are much needed to achieve a proper risk quantification for viral transmission during both laparoscopic and open surgical approaches. Based on 4 patients with intraperitoneal RNA detection, as opposed to millions of SARS-CoV-2 infections worldwide, we cannot encourage to perform open surgery instead of laparoscopy. Confirmation of effluent contagiousness was suggested before imposing specific procedures, as the dissemination risk during PD seems very low.<sup>10</sup> Transmission factors during surgery can be multifactorial, notably ventilation-associated factors in addition to peritoneal access-related ones, underlining the importance of general precautions recommended by surgical societies.

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## Conflicts of interest/Disclosure

The authors declare that they do not have any conflicts of interest.

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