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Original Article

Transmission of SARS-CoV-2 in Surgical Smoke during Laparoscopy: A Prospective, Proof-of-concept Study

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ABSTRACT **Study Objective:** There are growing concerns regarding the potential risk of coronavirus disease transmission during surgery and in particular during minimally invasive procedures owing to the aerosolization of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) particles. However, no study has demonstrated this hypothesis. Here, we aimed to investigate the presence of SARS-CoV-2 in surgical smoke.

Design: A prospective pilot study.

Setting: A tertiary cancer center in northern Italy.

Patients: Overall, 17 patients underwent laparoscopic procedures for the management of suspected or documented gynecologic malignancies. The median age was 57 years (range 26−77). The surgical indications included endometrial cancer (n = 11), borderline ovarian tumor (n = 3), early-stage ovarian cancer (n = 1), stage IA cervical cancer after diagnostic conization (n = 1), and an ovarian cyst that turned out to be benign at final histologic examination (n = 1).

Interventions: We evaluated all consecutive women scheduled to have laparoscopic procedures for suspected or documented gynecologic cancers. The patients underwent planned laparoscopic surgery. At the end of the laparoscopic procedures (after extubation), we performed reverse transcription−polymerase chain reaction (RT-PCR) tests for the detection of SARS-CoV-2 from both the endotracheal tube and the filter applied on the trocar valve.

Measurements and Main Results: In 1 patient, both swab tests (endotracheal tube and trocar valve filter) showed amplification of the *N* gene on RT-PCR analysis. This case was considered to be a presumptive positive case. In another case, the RT-PCR analysis showed an amplification curve for the *N* gene only in the swab test performed on the filter. No *ORF1ab* amplification was detected.

Conclusion: Our study suggested the proof of principle that SARS-CoV-2 might be transmitted through surgical smoke and aerosolized native fluid from the abdominal cavity. Journal of Minimally Invasive Gynecology (2021) 28, 1519−1525. © 2021 AAGL. All rights reserved.

Keywords: COVID-19; Gynecology; Surgery; Aerosolization

On December 31, 2019, in Wuhan, the capital of the province of Hubei in central China, hospitals recorded numerous cases of pneumonia of unknown cause, initially named "novel coronavirus pneumonia." On January 7, 2020, researchers identified a new coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) in the patients who had become infected, thanks to reverse transcription−polymerase chain reaction (RT-PCR) and next-generation sequencing techniques. On March 11, 2020, the World Health Organization formally declared the coronavirus disease (COVID-19) outbreak a pandemic, and on June 7, 2020, there were 6 799 713 cases of infections and 397 388 deaths worldwide [1].

COVID-19 has extremely high transmissibility levels [1]. The infection is mainly transmitted through droplets (≥5 μm in diameter) generated by the respiratory tract of a person who has become infected and expelled at short distances (<1 m), especially when coughing or sneezing, by both patients who are symptomatic and patients who are asymptomatic during the latency period of the disease. Owing to the risk associated with the aerosol transmission mode of COVID-19, a concern regarding the use of minimally

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invasive techniques and the creation of pneumoperitoneum has been raised [2,3].

The Society of American Gastrointestinal and Endoscopic Surgeons [2] was 1 of the first professional organizations to raise an alarm about the potential risk of COVID-19 transmission during surgery and in particular during laparoscopic or robotic procedures. Several statements recommended the adoption of protective equipment when performing minimally invasive procedures during the COVID-19 outbreak. Most of them reported very little evidence to support viral transmission through a minimally invasive approach and only recommended making modifications to surgical practice, such as using smoke evacuation, minimizing energy device use, reducing the number of healthcare staff, and shortening the occupation of the operating room (Op.R), especially during the intubation and extubation phases [3−5]. Although serval guidelines have warned against the execution of minimally invasive surgery in the COVID-19 era, this risk is hypothetical. In fact, no studies have evaluated the presence of SARS-CoV-2 in surgical smoke and aerosolized native fluid from the abdominal cavity.

In the present study, we aimed to assess the risk of transmission of SARS-CoV-2 through surgical smoke. As a secondary end point, we sought to identify the effectiveness of triage methods in identifying patients with COVID-19 before their admission to COVID-19−free hubs.

Materials and Methods

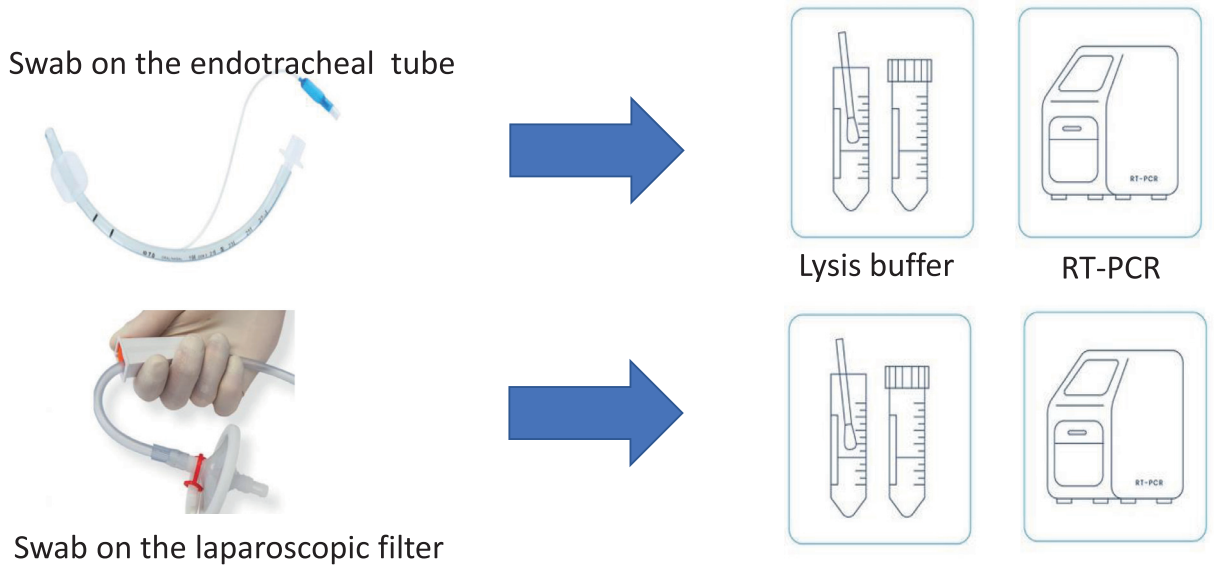
This prospective study was approved by the institutional review board of the Fondazione IRCCS Istituto Nazionale dei Tumori di Milano (Milan, Italy). During the COVID-19 outbreak, the Italian national healthcare system categorized hospitals as centers dedicated to the treatment of patients affected by COVID-19 and COVID-19−free hubs dedicated to the treatment (that cannot be postponed) of patients without SARS-CoV-2 infection [6−8]. The Fondazione IRCCS Istituto Nazionale dei Tumori di Milano is a comprehensive cancer center and a COVID-19−free hub dedicated to the treatment of patients with oncologic disease.

To reduce the in-hospital spread of COVID-19, the Fondazione IRCCS Istituto Nazionale dei Tumori di Milano adopted triage methods to identify patients affected by COVID-19. Only patients considered to be negative for COVID-19 were admitted to our center. In addition, a number of to-hospital and within-hospital filters were applied [8]. Following our institutional protocol, all patients admitted for surgery were clinically evaluated, and the collection of anamnestic data (e.g., history of fever, respiratory symptoms, and exposure to COVID-19) was accorded paramount importance. In addition, all patients scheduled for surgery had a high-resolution, low-dose computed tomography (CT) scan of the thorax (to rule out the presence of interstitial pneumonia), followed by an RT-PCR test for the detection of SARS-CoV-2 in the nasopharyngeal swabs whenever the CT scan was suggestive of a lung infection. Details of our triage protocol have been reported elsewhere [8].

The primary end point measure of this prospective study was to evaluate the presence of SARS-CoV-2 in the surgical smoke and pneumoperitoneum. All consecutive patients scheduled to have laparoscopic surgery for suspected or documented gynecologic malignancies were included in the present study. The study population included women undergoing laparoscopic surgery between April 1, 2020, and April 31, 2020. The other inclusion criteria included (1) age ≥18 years, (2) eligibility for surgical treatment, and (3) at least 30 days of follow-up. The patients signed a consent form for data collection for research purposes. According to the study protocol, patients having conversion to open surgery after a primary laparoscopic approach were excluded from the present investigation. The patients were admitted after having negative triage (anamnestic data and CT scan of thorax and/or nasopharyngeal swab test) results. The patients underwent planned laparoscopic surgery. All patients had general endotracheal anesthesia. The same team of expert surgeons performed all surgical procedures. Laparoscopic procedures were generally performed using a 4-port technique (a 10-mm optical port was placed in the umbilicus and 3 5-mm ancillary trocars were placed in the lower abdominal quadrants). When needed, a Clermont-Ferrant uterine manipulator (Karl Storz, Tuttlingen, Germany) was used. Pneumoperitoneum pressure was set at 12 mm Hg. A filter was applied to the trocar valve to avoid possible contamination of the staff working in the Op.R. For the same purpose, the staff used adequate personal protective equipment consisting of filtering surgical masks (filtering facepiece score: 2) and safety goggles. During the study period, there were no significant differences in the facilities available for patient care. Other aspects of patient management unrelated to the surgical approach remained consistent over time. The patients were catheterized with an indwelling Foley catheter for 1 to 2 days on the basis of the surgical complexity of the procedure. Operative times were recorded from the first skin incision to the last skin suture. The estimated blood loss was calculated from the contents of the suction devices. Hospital stay was counted from the first postoperative day. Intraoperative complications included any damage to surrounding structures, blood loss ≥1000 mL, and the need for blood transfusions. In-hospital postoperative complications were recorded from medical records, whereas complications that occurred after discharge were recorded at the time of readmission or follow-up visits. The grade of complication was assessed using the Accordion grading system [6]. For study purposes, we reported complication grade 3 or worse occurring within 30 days after surgery. At the end of the laparoscopic procedures (after extubation), we performed RT-PCR tests for the detection of SARS-CoV-2 on both the endotracheal tube and the filter applied on the trocar valve (Fig. 1). These were tested for 2 gene targets: *ORF1ab* and *N*. According to accumulative data regarding analysis of the SARS-CoV-2 genome, the *ORF* and *N* genes represent the

Fig. 1

Study design (*blue arrows*). RT-PCR = reverse transcription–polymerase chain reaction.



most specific targets for its detection [9,10]. The *ORF1ab* gene is highly presumptive for the presence of SARS-CoV-2, whereas the *N* gene might be detected even in other coronavirus infections [1,9,10]. The amplification curve of the *ORF1ab* gene suggested that 1 case was positive for SARS-CoV-2, whereas the amplification curve of the *N* gene suggested a presumptive positive case of SARS-CoV-2 (because the amplification curve of the *N* gene might be related to another coronavirus infection). The assay was performed according to the World Health Organization guidelines [1,9,10].

RNA was extracted using a QIAsymphony DSP Virus/Pathogen midi kit (Qiagen, Hilden, Germany) following the manufacturer's instructions. Sample inactivation was performed with treatment with Buffer ATL (Qiagen) and Proteinase K (Qiagen), followed by 15-minute incubation at 56°C. Tests were carried out with the VIASURE SARS-CoV-2 Real-Time PCR Detection Kit (CerTest Biotec, Zaragoza, Spain), which detects *ORF1ab* and *N* genes. The VIASURE kit includes a multiplex assay for 3 targets: (1) the viral *N* gene, (2) *ORF1ab* genes, and (3) a synthetic internal control. Lyophilized reaction wells were reconstituted with 15 μL of rehydration buffer, followed by the addition of 5 μL of the RNA sample. PCR reactions were performed using a QuantStudio 12K Flex Real-Time PCR System (Thermo Scientific, Waltham, MA). Data acquisition was performed using the QuantStudio 12K Flex software version 1.2.3 (Thermo Scientific), with automated threshold and baseline setting, followed by manual inspection of the individual amplification curves. Positivity to the RT-PCR assay was defined as specified in the manufacturer's instructions (IU-NCO2012enes0420 rev.01) imposing a cycle threshold value of <38. Descriptive statistics were used. Statistical analysis was performed using SPSS version 20.0 (IBM Corp., Armonk, NY).

Results

Over the study period, 52 patients underwent surgery at the gynecologic oncology unit of the Fondazione IRCCS Istituto Nazionale dei Tumori di Milano. Among those, 17 (33%) patients had a laparoscopic procedure for the management of suspected or documented gynecologic malignancies. Fig. 2 shows the study design. The baseline characteristics of the study population are presented in Table 1. The median age was 57 years (range 26–77). The surgical indications included endometrial cancer (n = 11), borderline ovarian tumor (n = 3), early-stage ovarian cancer (n = 1), stage IA cervical cancer after diagnostic conization (n = 1), and an ovarian cyst that turned out to be benign at final histologic examination (n = 1). The median operative time was 113 minutes (range 16–180). No conversion to open surgery occurred. No intraoperative or 30-day postoperative complication occurred. Table 2 shows the perioperative outcomes. In 1 patient, both swab tests (endotracheal tube and trocar valve filter) showed amplification of the *N* gene in the RT-PCR analysis. This case was considered to be a presumptive positive case. In another case, the RT-PCR analysis showed an amplification curve for the *N* gene only in the swab test performed on the filter. No *ORF1ab* amplification was detected. The postoperative course of those patients was unremarkable. They did not develop COVID-19–related symptoms, and they had negative

Fig. 2

Procedure for swab acquisition after laparoscopic surgery. COVID-19 = coronavirus disease 2019; CT = computed tomography; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

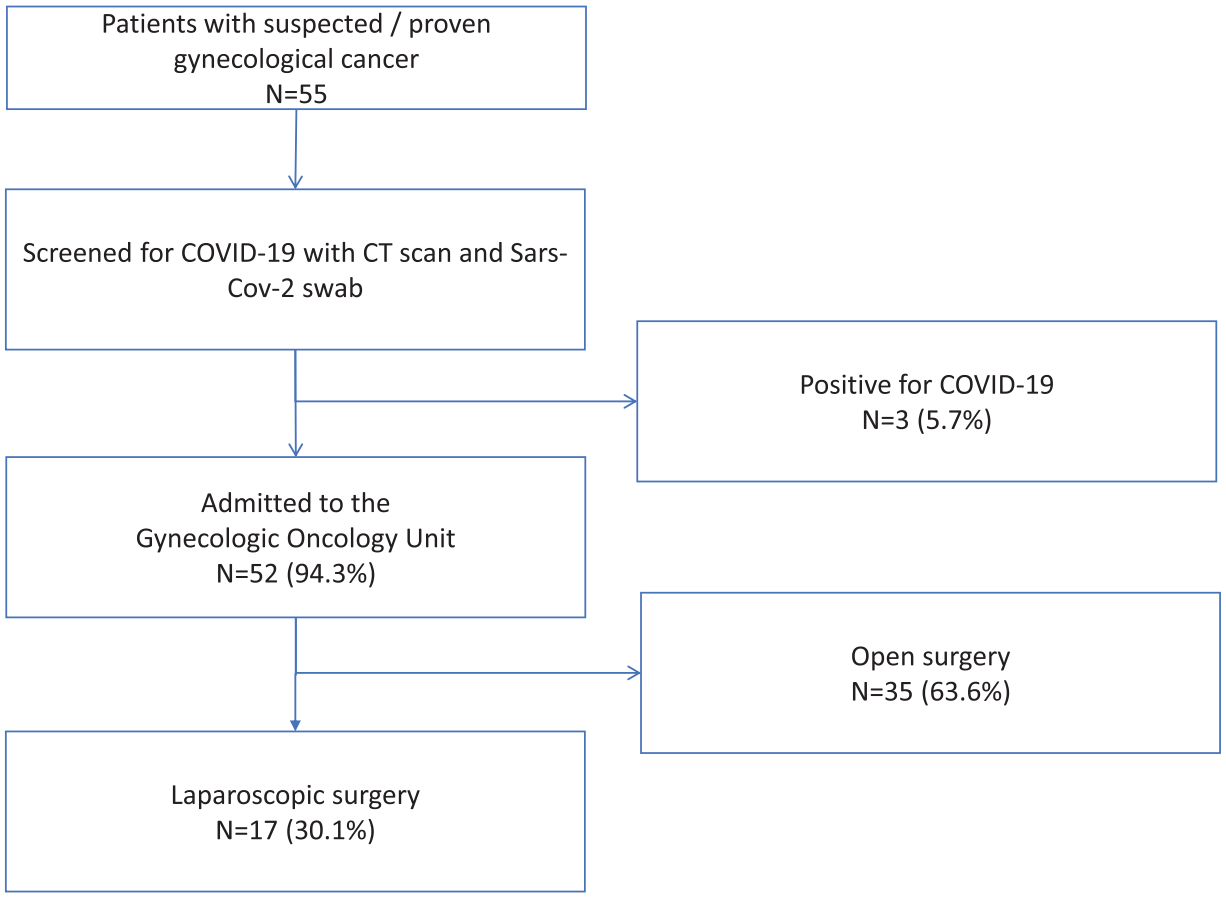


Table 1

Baseline characteristics of the study population (n = 17)

Characteristic	Number	%
Age, yrs	57 (26–77)	—
BMI, kg/m^2	26 (18–37)	—
Menopausal status		
No	4	23.5
Yes	13	76.5
ECOG		
ECOG 0	14	82.4
ECOG 1	2	11.8
ECOG 2	1	5.8
CCI		
CCI <3	11	64.7
CCI ≥3	6	35.3
Indications		
Endometrial cancer	11	64.8
Cervical cancer	1	5.8
Ovarian cancer	1	5.8
Borderline ovarian tumor	3	17.8
Ovarian benign lesion	1	5.8

BMI = body mass index; CCI = Charlson comorbidity index; ECOG = Eastern Cooperative Oncology Group.
Values are given in median (range) or number (%).

nasopharyngeal swab test results performed 1 week after surgery. Table 3 reports the results of the swab tests performed in every patient.

Discussion

The present paper evaluated the prevalence of SARS-CoV-2 infection in a COVID-19–free hub and evaluated the presence of SARS-CoV-2 particles in surgical smoke

Table 2

Surgery-related parameters

Characteristic	Value
Operative time, min	113 (16–180)
Estimated blood loss, mL	10 (10–100)
Laparotomic conversions	0
Hospital stay, d	2 (1–5)
Intraoperative complications	0
Intra- or postoperative transfusions	0
Postoperative complications (within 30 days)	0

Values are given in median (range) or number (%).

Table 3

Results of the swab tests

Age, yrs	BMI, kg/m^2	History of COVID-19	Surgical indication	Operative time, min	Hospital stay, d	Sample	RNA extraction	SARS-CoV -2	Ct: *N*	Ct: *ORF1ab*
58	31	Negative	Endometrial cancer	126	3	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
39	22	Negative	Endometrial cancer	115	2	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
71	23	Negative	Endometrial cancer	161	3	Smoke extractor	Yes	Additional confirmatory testing	35.22	Undetermined
						Endotracheal tube	Yes	Additional confirmatory testing	34.78	Undetermined
26	18	Negative	Borderline ovarian tumor	105	3	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
55	27	Negative	Borderline ovarian tumor	160	1	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
64	23	Negative	Endometrial cancer	117	3	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
23	19	Negative	Borderline ovarian tumor	60	2	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
31	24	Negative	Cervical cancer	65	1	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
78	23	Negative	Endometrial cancer	140	5	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
53	23	Negative	Endometrial cancer	16	2	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
77	22	Negative	Endometrial cancer	99	3	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
55	34	Negative	Endometrial cancer	109	5	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
75	27	Negative	Endometrial cancer	114	1	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
66	29	Negative	Endometrial cancer	110	1	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
54	37	Negative	Endometrial cancer	180	2	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
72	30	Negative	Ovarian myoma	107	5	Smoke extractor	Yes	Negative	42.72	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined
71	35	Negative	Endometrial cancer	135	5	Smoke extractor	Yes	Negative	Undetermined	Undetermined
						Endotracheal tube	Yes	Negative	Undetermined	Undetermined

COVID-19 = coronavirus disease; Ct = cycle threshold; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

and aerosolized native fluid from the abdominal cavity. The present study reported interesting findings. First, it is possible that SARS-CoV-2 might be transmitted through surgical smoke/aerosolized fluid. Second, although triage methods are effective in detecting patients with COVID-19, it is possible that nasopharyngeal swab tests and CT scans of the thorax failed to identify some patients with asymptomatic COVID-19.

The Food and Drug Administration continues to work with test developers to make more tests available [11]. The adoption of more accurate molecular diagnostic tests would be helpful in reducing the rate of false-negative results, thus minimizing the risk of in-hospital contamination.

There are growing concerns regarding the adoption of minimally invasive surgery during the COVID-19 pandemic. The accumulative evidence suggests that surgery must be avoided in patients with COVID-19 infection, and all nonurgent surgical treatments must be postponed. However, cancer management cannot be postponed. As aforementioned, several surgical societies expressed concerns about the likelihood of the Op.R staff's being affected by possible contamination during the outbreak. However, no studies demonstrated or denied this hypothesis. For the first time, in our study, we made an attempt to test this hypothesis. We observed a presumptive positive case in both endotracheal tube and laparoscopic filters, thus providing a clue to the possible risk of contamination during the COVID-19 pandemic.

Flemming et al [12] collected abdominal fluid (ascites), bile, liver, and gall bladder samples during emergency cholecystectomy performed in a patient who was critically ill with COVID-19. They observed that the PCR test revealed strongly positive results for SARS-CoV-2 RNA in the tracheal secretion, but all PCR tests performed on the abdominal samples were negative. Coccolini et al [13] reported a case of a patient affected by COVID-19 undergoing open surgery for bowel obstruction. In this case, SARS-CoV-2 was detected in the peritoneal fluid at a higher concentration than in the respiratory tract. This case corroborates our findings, suggesting the potential transmission of COVID-19 in surgical smoke during either minimally invasive or open abdominal procedures [13]. According to these findings, there is the potential for COVID-19 transmission with minimally invasive surgery and open surgery, but at least with minimally invasive surgery the smoke is contained and can be better controlled than with open surgery where most of the smoke is dispersed into the Op.R. We have to stress this point to the surgical community to improve the protection of the Op.R staff. The main weaknesses of the study included the inherent biases of the small sample size and the single-centre nature of our investigation. However, the prospective study design represents the main strength of our investigation.

Two points of this study have to be addressed. First, during the study period (at the beginning of the COVID-19 outbreak in Italy) all patients presenting at the Fondazione IRCCS Istituto Nazionale dei Tumori di Milano were triaged with clinical evaluation, blood test, and low-dose CT scan of the thorax. The objective was to avoid surgery in patients with pneumonia. In May 2020, we started to adopt nose-throat swab tests for COVID-19 in all patients. Second, this study reports our preliminary experience in evaluating the presence of SARS-CoV-2 in surgical smoke and aerosolized native fluid from the abdominal cavity. During the second wave of the pandemic, we plan to test only patients who have recovered from COVID-19 infection to evaluate the possible persistent presence of SARS-CoV-2 in the blood and abdominal fluids.

In conclusion, the present study provides evidence suggesting a potential new method of transmission of COVID-19. Personal protective equipment must be worn to reduce contamination risks for healthcare providers. The Op.R staff needs protection. However, minimally invasive surgery should not be ruled out during the COVID-19 outbreak. Open surgery is related to an increased risk of developing postoperative morbidity and longer length of hospital stay compared with a minimally invasive approach [14]. Potentially, a laparoscopic approach might improve postoperative recovery, thus reducing postoperative events (including pneumonia) in patients harboring SARS-CoV-2 infection. Prioritizing patients' health and welfare during the COVID-19 outbreak is of paramount importance. Further evidence is needed to better understand the possible methods of transmission of COVID-19.

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References

1. Indini A, Rijavec E, Ghidini M, et al. Coronavirus infection and immune system: an insight of COVID-19 in cancer patients. *Crit Rev Oncol Hematol*. 2020;153:103059.
2. Pryor A. Sages and EAES recommendations regarding surgical response to COVID-19 crisis. Available at: https://www.sages.org/recommendations-surgical-response-covid-19/. Accessed April 23, 2020.
3. Bogani G, Raspagliesi F. Minimally invasive surgery at the time of COVID-19: the OR staff needs protection. *J Minim Invasive Gynecol*. 2020;27:1221.
4. Bogani G, Casarin J, Pinelli C, et al. Management of patients with ovarian cancer in the COVID-19 era. *J Surg Oncol*. 2020;122:122–123.
5. Morris SN, Fader AN, Milad MP, Dionisi HJ. Understanding the "scope" of the problem: why laparoscopy is considered safe during the COVID-19 pandemic. *J Minim Invasive Gynecol*. 2020;27:789–791.
6. Bogani G, Ditto A, Bosio S, Brusadelli C, Raspagliesi F. Cancer patients affected by COVID-19: experience from Milan. *Lombardy. Gynecol Oncol.* 2020;158:262–265.
7. Bogani G, Brusadelli C, Guerrisi R, et al. Gynecologic oncology at the time of COVID-19 outbreak. *J Gynecol Oncol*. 2020;31:e72.
8. Valenza F, Papagni G, Marchianò A, et al. Response of a comprehensive cancer center to the COVID-19 pandemic: the experience of the Fondazione IRCCS-Istituto Nazionale dei Tumori di Milano. *Tumori*. 2020 May 4. [Epub ahead of print].

9. Raza H, Wahid B, Rubi G, Gulzar A. Molecular epidemiology of SARS-CoV-2 in Faisalabad, Pakistan: a real-world clinical experience. *Infect Genet Evol*. 2020;84:104374.
10. Laamarti M, Alouane T, Kartti S, et al. Large scale genomic analysis of 3067 SARS-CoV-2 genomes reveals a clonal geo-distribution and a rich genetic variations of hotspots mutations. *PLoS One*. 2020;15:e0240345.
11. U.S. Food and Drug Administration. Coronavirus disease 2019 testing basics. Available at: https://www.fda.gov/consumers/consumer-updates/coronavirus-disease-2019-testing-basics. Accessed December 15, 2020.
12. Flemming S, Hankir M, Hering I, et al. Abdominal fluid samples (negative for SARS-CoV-2) from a critically unwell patient with respiratory COVID-19. *Br J Surg*. 2020;107:e259–e260.
13. Coccolini F, Tartaglia D, Puglisi A, et al. SARS-CoV-2 is present in peritoneal fluid in COVID-19 patients. *Ann Surg*. 2020;272:e240–e242.
14. Bogani G, Borghi C, Leone Roberti Maggiore U, et al. Minimally invasive surgical staging in early-stage ovarian carcinoma: a systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2017;24:552–562.