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Is There a Risk of Virus Contamination Through Pneumoperitoneum During Laparoscopic Surgery in Patients with COVID-19? A Cadaveric Study.

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Dear Editor,

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease it causes, coronavirus disease 2019 (COVID-19), are causing a dramatic pandemic infection, severely affecting clinical practice worldwide. Despite the lack of complete understanding of polymorphous clinical presentation of COVID-19, recommendations from world health authorities to surgical societies have been published in order to prevent viral transmission within the hospital setting. In this scenario, a panel of Italian urologists has agreed on possible strategies for the reorganization of urological routine practice and on a set of recommendations that should facilitate the process of rescheduling both surgical and outpatient activities during the COVID-19 pandemic and in the subsequent phases, identifying non-deferrable, semi-non-deferrable and deferrable interventions [1].

Concerning minimally invasive surgery (MIS), main national and international surgical associations, suggested caution or even discouraged the use of laparoscopy due to a theoretical risk of virus spread through pneumoperitoneum aerosol (PA) [2-3], although no studies have ever investigated any type of coronavirus and no cases of SARS-CoV-2 contagion related to PA have been reported. On the other hand, the advantages of MIS are well documented, such as short hospitalization and higher precision of surgical maneuvers with improved oncological and functional outcomes [4-5].

In the light of this, we aimed to assess the risk of virus spread due to PA for healthcare workers during laparoscopic procedures through a cadaveric model, performed on patients who died from COVID-19.

From June 2020 to January 2021, twelve cadavers were enrolled. The research protocol was approved by the Institutional Review Board (2020/ST/143).

All patients had SARS-CoV-2 infection confirmed by real-time PCR analysis of nasopharyngeal swab samples collected at the time of hospital admission, and all had undergone molecular tests for common respiratory viruses and bacteria by the microbiology laboratories, with negative results.

The laparoscopic instruments included 5 mm trocars with a flap valve (Ultimate dilating tip trocars; Purple Surgical, Shenley, UK); high-flow insufflation unit (Electronic endoflator; Karl Storz, Tuttlingen, Germany); pneumoperitoneum smoke evacuation system (SES) (Smoke filter; Purple Surgical, Shenley, UK).

A supraumbilical 5 mm trocar (Tr1) was placed setting the pneumoperitoneum to 18 mmHg. A second 5 mm trocar (Tr2) was placed at least 10 cm from Tr1 connected to the SES (Fig. 1). Four samples were taken during the procedure: one from nasopharynx (S1); one from Tr2 after insufflation closure until a complete desufflation of the abdomen (S2); one represented by the internal membrane of SES after pneumoperitoneum induction and a complete deflation (S3); one from the abdomen through the Tr1 passage after trocars removal and pneumoperitoneum deflation without use of the filtration system (S4). Lung, kidney and liver specimens were analyzed using molecular biology for SARS-CoV-2 detection.

Patients' characteristics are reported in Table 1, with a mean age of 78.2 years (SD 8.3; range 61-89). Reported causes of death were septic multi-organ failure, respiratory failure, intestinal ischemia in 7 (58.3%), 4 (33.3%) and 1 (8.3%) cases, respectively; whereas mean time from death to procedure was 1.5 days (SD 0.7; range 0.5-2.8). S1 resulted positive in 8 (66.7%) cases, while no positivity was encountered for S2, 3, or 4. Analysis from lung, kidney and liver specimens resulted positive in 66.7%, 60% and 20% of cases, respectively.

In our model, S1, kidney, liver and lung samples were intended to confirm SARS-CoV-2 infection. Since laparoscopy was deemed to be an aerosol generating procedure (AGP) in several situations, such as deflation of pneumoperitoneum without use of a filtration system, specimen extraction, and leakage of CO₂ from inaccurately sized incision ports [4], several maneuvers were emphasized in order to increase the likelihood of positiveness of our samples. Accordingly, a high pneumoperitoneum pressure (18 mmHg) was set in order to increase the output gas on the swab [6]. In addition, S2, S3 and S4 were collected to identify the virus through different hypothetical contamination modalities: S2 simulates the introduction of an instrument through a trocar, as it would normally occur during a laparoscopy; S3 corresponds to the analysis of the SES internal membrane which guarantees 99.999% bacterial and viral particles filtration efficiency; whereas, S4 was taken on Tr1 passage after trocars removal and pneumoperitoneum deflation without use of a filtration system, a well known AGP.

A recent report from Zheng *et al.* [6] highlighted a higher risk of contagion for laparoscopic surgery, due to higher particles of the surgical smoke and the risk of aerosol dispersal through pneumoperitoneum leakage,

consequently advocating special caution, including minimizing the use of electrocautery, reduction of pneumoperitoneum pressure and generous use of suction devices.

A well-designed systematic review performed by Pavan *et al.*, reported no studies conducted on any coronavirus. To date, the recommendations of surgical societies are based on speculations about studies conducted on the human papillomavirus and the hepatitis B virus. The authors conclude that, not being able to exclude the risk of a virus spread through surgical smoke, the adoption of all protective strategies is mandatory, advocating the need to conduct specific clinical or preclinical studies on SARS-CoV-2 [2].

In order to reduce SARS-CoV-2 contagion during laparoscopic procedures, the latest Society American Gastrointestinal and Endoscopic Surgeons (SAGES) and European Association for Endoscopic Surgeons (EAES) Guidelines recommended the use of devices to filter released CO₂ for aerosolized particles, the reduction of medical staff to the minimum inside the operating room, and the use of personal protective equipment [4]. On the other side, a more prudent attitude regarding laparoscopy has been adopted by the Intercollegiate General Surgery Guidance in the United Kingdom, relegating laparoscopy to selected individual cases, where the clinical patient's benefit exceeds the risk of potential viral transmission. Moreover, Di Saverio *et al.* raised important concern about the potential risks of viral spread, thus avoiding pursuing laparoscopy at all costs [7].

Despite the introduction of vaccines against SARS-CoV-2, non-cancer-related surgical procedures are still discouraged, whereas oncological interventions have been delayed due to medical and paramedical staff reallocation to face the emergency, with a reduced availability of intensive care beds. Therefore, MIS with its well-documented advantages could represent a valid ally for the optimization of available beds.

Our results are to be interpreted with respect to their limitations, deriving from a prospective analysis of the data collected on a small cohort. Therefore, an external validation with an independent, larger and more diversified samples would be required.

In conclusion, the present model showed no evidence of SARS-CoV-2 from the gas evacuated during an induced pneumoperitoneum in COVID-19 cadavers. If these findings will be confirmed by larger clinical studies, the laparoscopic and robotic approaches could be safely used in COVID-19 patients with all the benefits of MIS.

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Table 1. Patients' characteristics.

Patient no.	Age (y)	Time of hospitalization (d)	Time from symptom onset to death (d)	Cause of death	Time from death to procedure (h;m)	S1	S2	S3	S4	Lung	Kidney	Liver
1	80	26	15	septic MOF	15;20	P	N	N	N	P	N	N
2	76	6	19	respiratory failure	13;10	N	N	N	N	P	P	N
3	61	21	37	septic MOF	67;50	N	N	N	N	N	N	N
4	86	2	7	respiratory failure	47;30	P	N	N	N	MD	P	N
5	84	1	6	respiratory failure	26;30	P	N	N	N	MD	P	P
6	73	23	30	septic MOF	24;10	N	N	N	N	MD	MD	MD
7	75	2	4	respiratory failure	54;20	N	N	N	N	MD	MD	MD
8	79	9	13	septic MOF	24;45	P	N	N	N	MD	MD	MD
9	89	4	18	septic MOF	42;20	P	N	N	N	MD	MD	MD
10	87	10	17	septic MOF	42;30	P	N	N	N	MD	MD	MD
11	70	3	10	septic MOF	24;57	P	N	N	N	MD	MD	MD
12	78	4	9	intestinal ischemia	34;20	P	N	N	N	MD	MD	MD

Legend: y=year-old; d=days; h= hours; m=minutes; MOF= multi-organ failure; S1= sample 1; S2= sample 2;

S3= sample 3; S4= sample 4; P= positive for SARS-CoV-2; N= negative for SARS-CoV-2; MD= missing data

Figure 1. Cadaveric model. Supraumbilical open access was made to insert a 5 mm disposable trocar (Tr1); after induction of 18 mmHg pneumoperitoneum a second 5 mm disposable trocar (Tr2) was placed 10 cm from the patient's midline between Tr1 and left anterior superior iliac spine and a pneumoperitoneum smoke evacuation system was connected to Tr1.

Author contributions

Conceptualization: Gregori Andrea, Antonio Maria Granata. Data curation: Antonio Maria Granata, Claudio Fenizia, Franco Palmisano, Ai Ling Loredana Romanò, Michele Talso, Roberta Simona Rossi. Formal analysis: Andrea Gregori, Antonio Maria Granata, Claudio Fenizia. Investigation: Andrea Gregori, Antonio Maria Granata, Roberta Simona Rossi, Claudia Vanetti, Cristina Tonello, Claudio Fenizia, Luca Carsana, Pietro Zerbi, Methodology: Antonio Maria Granata, Andrea Gregori. Supervision: Andrea Gregori, Manuela Nebuloni, Daria Trabattoni. Validation: Andrea Gregori, Manuela Nebuloni, Daria Trabattoni. Writing – original draft: Franco Palmisano. Writing – review & editing: Franco Palmisano, Andrea Gregori, Antonio Maria Granata, Claudio Fenizia, Roberta Simona Rossi.

