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Risk of Virus Contamination Through Surgical Smoke During Minimally Invasive Surgery: A Systematic Review of the Literature on a Neglected Issue Revived in the COVID-19 Pandemic Era

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Abstract

Context: The coronavirus disease 2019 (COVID-19) pandemic raised concerns about the safety of laparoscopy due to the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) diffusion in surgical smoke. Although no case of SARS-CoV-2 contagion related to surgical smoke has been reported, several international surgical societies recommended caution or even discouraged the use of a laparoscopic approach.

Objective: To evaluate the risk of virus spread due to surgical smoke during surgical procedures.

Evidence acquisition: We searched PubMed and Scopus for eligible studies, including clinical and preclinical studies assessing the presence of any virus in the surgical smoke from any surgical procedure or experimental model.

Evidence synthesis: We identified 24 studies. No study was found investigating SARS-CoV-2 or any other coronavirus. About other viruses, hepatitis B virus was identified in the surgical smoke collected during different laparoscopic surgeries (colorectal resections, gastrectomies, and hepatic wedge resections). Other clinical studies suggested a consistent risk of transmission for human papillomavirus (HPV) in the surgical treatments of HPV-related disease (mainly genital warts, laryngeal papillomas, or cutaneous lesions). Preclinical studies showed conflicting results, but HPV was shown to have a high risk of transmission.

Conclusions: Although all the available data come from different viruses, considering that the SARS-CoV-2 virus has been shown in blood and stools, the theoretical risk of virus diffusion through surgical smoke cannot be excluded. Specific clinical studies are needed to understand the effective presence of the virus in the surgical smoke of different surgical procedures and its concentration. Meanwhile, adoption of all the

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required protective strategies, including preoperative patient nasopharyngeal swab for COVID-19, seems mandatory.

**Patient summary:** In this systematic review, we looked at the risk of virus spread from surgical smoke exposure during surgery. Although no study was found investigating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or any other coronavirus, we found that the theoretical risk of virus diffusion through surgical smoke cannot be excluded.

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1. **Introduction**

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease it causes, coronavirus disease 2019 (COVID-19), are causing a rapid and tragic health emergency worldwide. This is reshaping the health systems in several countries, due to the need to dedicate significant medical resources to the assistance of critically ill COVID-19 patients, with substantial implications also on the medical disciplines not primarily involved in the management of COVID-19 patients. Specifically, the vast majority of the centers in the areas more severely hit by the pandemic are limiting their surgical activities, according to specific recommendations for patient triage from international societies and independent research groups [1–5]. Concerning surgery, Zheng et al [6] recently reported recommendations for laparotomic and laparoscopic surgery to prevent the risk of aerosol dispersal containing viruses. Specifically, surgical smoke was considered to pose a risk of including active virus, and laparoscopic surgery was considered to increase the risk of contagion due to higher particles of the surgical smoke and the risk of aerosol dispersal through pneumoperitoneum leakage. Consequently, the authors recommended special attention, including minimizing the use of electrocautery, reduction of pneumoperitoneum pressure, and generous use of suction devices to remove smoke and aerosol during operations, especially before converting from laparoscopy to open surgery or any extraperitoneal maneuver [6]. Although, to our knowledge, no case of SARS-CoV-2 contagion related to those mechanisms has been reported during surgical procedures, several international surgical societies recommended caution or even discouraged the use of a laparoscopic approach during the pandemic [7–11].

The issue of the potential risk of surgical smoke has mostly been neglected in surgery in the last decades. However, it is becoming popular due to the present pandemic. Consequently, we elected to perform a systematic review of the literature evaluating the risk of virus spread due to surgical smoke for health care workers during surgical procedures (of any surgical specialties and for any clinical indications) performed on patients with a viral disease. Moreover, we also elected to collect all the experimental studies where surgical smoke in the same clinical situations was evaluated to detect the presence of any virus remnants and/or its ability to spread virus contagion.

2. **Evidence acquisition**

The request for registration of the present systematic review was submitted on April 2, 2020 to PROSPERO (Reg. CRD42020177934). The systematic review of the literature was performed on April 2, 2020 on PubMed and Scopus databases. The PubMed search used a complex search strategy, including both medical subject heading (MeSH) and free text protocols. Specifically, the MeSH search was conducted by combining the following terms retrieved from the MeSH browser provided by PubMed: "Infectious Disease Transmission, Patient-to-Professional," "Infectious Disease Transmission, Professional-to-Patient," "Health Personnel," "Viruses," "Bariatric Surgery," "Vitreoretinal Surgery," "Orbogastic Surgery," "Surgery, Plastic," "Surgery, Oral," "Colorectal Surgery," "Ambulatory Surgical Procedures," "Piezosurgery," "Dermatologic Surgical Procedures," "Urologic Surgical Procedures, Male," "Orthopedic Procedures," "Nasal Surgical Procedures," "Reconstructive Surgical Procedures," "Obstetric Surgical Procedures," "Robotic Surgical Procedures," "Minimally Invasive Surgical Procedures," "General Surgery," "Surgical Procedures, Operative," "surgery." Multiple “free text” searches were also performed, searching for the following terms individually in all fields of the records: "surgical hazard," "surgical byproducts," "surgical smoke," and "virus". Subsequently, the search results were pooled, applying no limitations. The searches on Scopus used only the free text protocol, with the same keywords. Subsequently, the query results were pooled without applying any limit.

Four of the authors reviewed the titles and abstracts of all the records to select the papers relevant to the review topic. Subsequently, the selected papers were assessed in full-text format by two other authors to collect all the relevant data. Specifically, we elected to collect all the clinical studies evaluating any surgical treatment for any patients with a viral disease where a risk of virus contagion was reported for the health workers. Moreover, we collected all the experimental studies where surgical smoke was evaluated to detect the presence of any virus remnants and/or its ability to spread virus contagion. Finally, we also included relevant studies identified from the reference list of the papers identified in our systematic search.

An electronic spreadsheet was designed by one of the authors for data extraction, which was performed independently by two other authors and completely double-checked by a further one.
Risk of bias of the available studies was estimated by questions #4 and #8–11 for clinical studies and by questions #1, #2, and #5–11 for preclinical studies from the National Toxicology Program/Office of Health Assessment and Translation (NTP/OHAT) Risk of Bias Rating Tool for Human and Animal Studies [12]. The study complied with the recently reported Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [13].

3. Evidence synthesis

3.1. Results

A total of 1064 records were retrieved from PubMed and 569 from Scopus. Fig. 1 summarizes the literature review process, which allowed the identification of 24 papers, including 14 clinical studies [14–27], eight preclinical studies [28–35], and two papers reporting both clinical and preclinical data [36,37].

3.1.1. Clinical studies

Kwak et al [27] reported on 11 patients who underwent a variety of laparoscopic and robotic procedures (including colorectal resections in five cases, gastrectomies in three cases, and hepatic wedge resections in another three cases). Preoperatively, all these patients had positive hepatitis B surface antigen (HBsAg), two had detectable hepatitis B surface antibody (HBsAb), two were positive for hepatitis B e antigen, and three patients were taking anti–hepatitis B viral medications at the time of the study. The surgical smoke produced during the different laparoscopies was collected and analyzed for the presence of hepatitis B virus (HBV) DNA. The polymerase chain reaction allowed the identification of HBV DNA in 10 of the 11 patients.

All the other clinical studies were focused on human papillomavirus (HPV) infection, and most of the available evidence highlighted a possible risk of contagion. Specifically, Glover and Roenigk [19] reported a survey of 4200 laser surgeons. The prevalence and localization of their lesions were compared with those of the patients observed in two population-based cohorts (patients with warts in Olmsted County and at the Mayo Clinic from 1988 to 1992). On the whole, the overall risk of the surgeons to acquire warts was similar to that of the general population. However, the prevalence of nasopharyngeal localization was significantly higher in laser surgeons, suggesting a specific risk for the upper airway mucosa due to laser plume. In another survey, Lobracco et al [22] reported that the overall incidence of HPV-related lesions was 3.2% among laser surgeons treating verrucae with the CO₂ laser, with the highest incidence being observed for hand lesions in dermatologists (15.2%). In the vast majority of the other reports aiming at the evaluation of the presence of HPV in surgical smoke, HPV was identified in most of the dermatology and gynecology reports [15,25,26,36,37]. Only three small studies failed to identify the virus in surgical byproducts [14,20,21]. Moreover, two other studies identified HPV DNA on samples from the nasolabial fold, nostrils, and conjunctiva of the surgeons as well as on the surgical gloves following laser ablation of laryngeal papillomas and genital warts [18–24].

3.1.2. Preclinical studies

Again, the majority of the preclinical studies were focused on HPVs and bovine papillomaviruses, with conflicting results. Specifically, some studies evaluating the presence of viral DNA in the surgical smoke after laser treatments of infected cell cultures reconfirmed the presence of the virus
| Reference | Study design | Cases | Specialty | Disease | Surgery performed | Energy | Methods | Endpoint | Results |
|-----------|--------------|-------|-----------|---------|------------------|--------|---------|----------|---------|
| Garden (1988) [36] | Prospective | 7 | Dermatology | Plantar or mosaic Verrucae | Ablation | CO₂ laser | Vapor was collected in a chamber in line with a vacuum system. Hybridization with HPV DNA probes revealed intact virus | To determine whether intact papillomavirus DNA exists in the plume of smoke during CO₂ laser treatment | Viral DNA was detected in the collected laser vapor from two of seven patients |
| Sawchuk (1989) [37] | Prospective | 8 | Dermatology | Plantar warts | Ablation | CO₂ laser vs electrocoagulation | Collection of the smoke produced in the 2 procedures | HPV DNA in vapor from human plantar warts Tested whether placing a surgical mask in the vapor path could inhibit the passage of the virus onto the collection filter | Greater amount of papillomavirus DNA was usually recovered in the laser vapor than in the electrocoagulation vapor from the same wart. A surgical mask was found capable of removing virtually all laser- or electrocoagulation-derived virus |
| Abramson (1990) [14] | Prospective | 7 | Otorhinolaryngology | Laryngeal papilloma | Laser ablation | CO₂ laser | Collection of plumes and DNA extraction | To detect viral DNA in the plumes of smoke generated by CO₂ laser treatment of warts | No detection of HPV DNA in the smoke plume unless direct suction contact is made with the papilloma tissue during surgery |
| Andre (1990) [15] | Prospective | 3 | Dermatology | Large genital condyloma | Laser ablation | CO₂ laser | Collection of plumes and DNA extraction | To detect viral DNA in the plumes of smoke generated by CO₂ laser treatment of warts | HPV DNA detected in 2 out of 3 plume collections |
| Ferenczy (1990) [16] | Prospective | 43 | Gynecology | Condyloma acuminatum in 26 patients and low- and high-grade intraepithelial lesions in the remaining 17 patients | Laser vaporization | CO₂ laser | Swabs from lesional tissues of 43 patients as well as from the treated areas and from the 5 cm surrounding normal skin before and after laser vaporization | Dispersal of viral DNA during laser therapy | 65 of 110 (60%) swabs of histologically unequivocal condylomata and cervical intraepithelial neoplasia Treatment fields and the surrounding 5 cm laser margins after vaporization yielded similar HPV DNA positivity (16%) |
| Reference          | Study design    | Cases | Specialty     | Disease                  | Surgery performed                                      | Energy          | Methods                          | Endpoint | Results                                                                 |
|--------------------|-----------------|-------|---------------|--------------------------|-------------------------------------------------------|-----------------|---------------------------------|----------|--------------------------------------------------------------------------|
| Hallmo (1991)      | Case report     | 1     | Otorhinolaryngology | Laryngeal papillomatosis | Removal from each vocal cord with a CO₂ laser         | Nd:YAG laser   | NA                              | NA       | Single case of 44-yr-old laser surgeon presented with laryngeal papillomatosis after laser treatment of 55 cancers in the distal colon and rectum, but also 5 patients with anogenital condyloma acuminate |
| Bergbrant (1994)   | Prospective     | 30    | Dermatology   | Genital warts            | Electrocoagulation                                   | Samples from nasolabial fold, nostril, and conjunctiva before and after the procedure PCR identification of the virus DNA | Contamination of personnel in the operating theater | Positive samples in 9/19 (47%) medical personnel after electrocoagulation vs 6/11 (54%) after laser ablation Two nasolabial fold samples were positive before electrocoagulation |
| Gloster (1995)     | Retrospective comparative | 31 surgeons vs 6124 patients | Dermatology | Warts in different sites | Laser vaporization                                   | CO₂ laser       | Clinical diagnosis in surgeons vs patients in population-based studies | Risks to surgeons of acquiring warts from the CO₂ laser plume vs risk of population CO₂ laser surgeons are no more likely to acquire nasopharynx warts than a person in the general population; less likely for other wart location |
| Capizzi (1998)     | Prospective     | 13    | Plastic surgery | Aesthetic reasons        | Laser resurfacing in the periorbital, perioral, or full-face regions | CO₂ laser (TruPulse laser) | Collection of the laser plume smoke for cultures by a filter in the smoke evacuator | To investigate the potential bacterial and viral exposure to operating room personnel as a result of the laser smoke plume in CO₂ laser resurfacing Each of the 13 patients had one bacterial, one viral, and one control culture (total 39 specimens) | No viral growth |
| Hughes (1998)      | Prospective     | 5     | Dermatology   | Clinically typical verrucae vulgares of the extremities | Laser ablation                                       | Erbium:YAG laser | Laser plume was deposited on the handpiece as an abundant fluffy material and was submitted for evaluation of HPV DNA by PCR | To determine the presence or absence of HPV DNA in the laser plume of erbium: YAG laser–treated human warts | HPV DNA was not detected in the erbium: YAG laser plume |
| Reference        | Study design | Cases | Specialty               | Disease                        | Surgery performed          | Energy    | Methods                                                                 | Endpoint                                                                 | Results                                                                 |
|------------------|--------------|-------|-------------------------|--------------------------------|------------------------------|-----------|-------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Lobraico (1988)  | Retrospective| 794   | Multispecialty          | HPV lesions                    | Laser ablation               | CO₂ laser | Clinical survey to define the type of laser used, number of years using the laser, presence or absence of lesions, and the location and biopsy confirmation of a lesion if present. If an acquired lesion was reported, a second in-depth questionnaire was distributed to determine the protective measures taken. After the responses to the second questionnaire were received, a telephone query was conducted with each positive respondent to substantiate the details of the questionnaire and to obtain further details. | To explore both the incidence of acquired lesions among laser users and the details predisposing to the development of such lesions. | The overall incidence of HPV-related lesions was 26/794 or 3.2% of those laser users treating verrucae with CO₂ laser. The highest incidence of acquired lesions among laser users was observed in dermatologists (17/112 or 15.2%), mainly with hand lesions. |
| Calero (2003)     | Case report  | 1     | Otorhinolaryngology     | Recurrent laryngeal papillomatosis | Excision of anogenital condylomas | Electrosurgical and laser surgical | NA        | NA                                                                     |                                                                        | Single case of a gynecology nurse who had assisted in electrosurgery and laser surgical ablation of anogenital condylomas and developed recurrent laryngeal papillomatosis. |
| Ilmarinen (2012)  | Prospective  | 10    | Otorhinolaryngology/dermatology | Laryngeal papillomas and genital warts | Surgical removal and laser vaporization | CO₂ laser | Sample of oral mucosa, surgical gloves, and face masks of health care personnel. PCR identification of the virus DNA. Risk of HPV transmission from the patient to the protective surgical masks, gloves, and oral mucosa of medical personnel. | Surgical gloves positive for 1 surgeon and 3 nurses in 5 laryngeal papillomas. Surgical gloves positive in all the operators in 5 of genital warts. All oral mucosa samples tested negative. All the surgical mask specimens tested negative. |                                                                        |
Table 1 (Continued)

| Reference          | Study design | Cases | Specialty | Disease                  | Surgery performed | Energy                          | Methods                                                                 | Endpoint                                                                 | Results                                                                                                                                 |
|--------------------|--------------|-------|-----------|--------------------------|-------------------|--------------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Neumann (2018)    | Prospective  | 4     | Gynecology| Cervix uteri HPV-related lesions | Loop electrosurgical excision | Laser ablations and loop electrosurgical excision procedures | The primary outcome was defined as HPV subtype in resected cone and in surgical plume resulting from LEEPs of high-grade squamous intraepithelial lesions of the cervix uteri. | To evaluate whether surgical plume resulting from routine LEEPs indicated contamination with high-risk HPV and showed the same HPV subtype as identified in the resected cones. | Four samples of surgical plume resulting from routine LEEPs indicated contamination with high-risk HPV and showed the same HPV subtype as identified in the resected cones. |
| Zhou (2019)       | Prospective  | 134   | Gynecology| CIN II-III lesions, persistent CIN I lesions, or chronic cervicitis with persistent high-risk HPV infections and continuous postcoital bleeding | Loop electrosurgical excision | Electrosurgery with high-frequency electrical generator and wire loop electrodes | Collection of the smoke plume generated by LEEP from the surgical site Preoperative and postoperative nasal swab specimens were collected from the surgeons for the detection of HPV DNA. | To investigate the prevalence of HPV DNA in LEEP plume, to confirm whether HPV DNA in surgical smoke leads to HPV infection in surgeons’ nasal cells and to demonstrate whether HPV DNA persists in the nasopharynx of these doctors. | 40/134 (29.9%) surgical smoke samples were positive for HPV DNA 2/134 (1.5%) of the nasopharynx swab of the surgeons after operation positive for HPV (70.1% wearing ordinary mask, 29.9% a special N95 surgical mask) Genotypes detected in cervical cells and surgical smoke were identical. The 2 operators with positive swab were wearing an ordinary mask. |
| Kwak (2016)       | Prospective  | 11    | Surgery   | Various conditions in HBV-infected patients | 5 lap/robotic colorectal resections 3 lap hepatic wedge resections 3 lap gastrectomy | Not reported | A collector was used to obtain surgical smoke in the form of hydrosol. The smoke was analyzed using nested PCR | Detection of HBV in surgical smoke | HBV was detected in surgical smoke in 10 of the 11 cases. |

CIN = cervical intraepithelial neoplasia; HPV = human papillomavirus; lap = laparoscopic; LEEP = loop electrosurgical excision procedure; NA = not available; PCR = polymerase chain reaction.
| Reference        | Study design | Sample size | Disease                  | Procedure              | Energy       | Methods                                                                 | Endpoint                                                                 | Results                                                                 |
|------------------|--------------|-------------|--------------------------|------------------------|--------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Garden (1988) [36] | Prospective  | 4           | Bovine papillomas        | Ablation               | CO₂ laser    | Vapor was collected in a chamber in line with a vacuum system. Hybridization with bovine papillomavirus DNA probes revealed intact bovine papillomavirus | To determine whether intact papillomavirus DNA exists in the plume of smoke during CO₂ laser treatment | Bovine papillomavirus DNA was detected in the plume of smoke in three of the four treated fibropapillomas |
| Sawchuk (1989) [37] | Prospective  | 1           | Bovine papillomas        | Bovine wart            | CO₂ laser vs electrocoagulation | Collection of the smoke produced | Products of the laser vapor induced foci of morphologically transformed cells and cells containing BPV-I DNA |
| Wisniewski (1990) [28] | Prospective  | 10          | Cervical lesion          | Ablation of cervical mucosa in patients | CO₂ laser    | Collection of the airborne particulate and culture                     | Southern blot testing of laser ejecta                                  | Absence of viral organisms                                               |
| Kunachak (1996) [29] | Prospective  | 10          | Recurrent respiratory papillomatosis | Laser ablation         | CO₂ laser    | Collection of the laser plume                                          | To determine the potential risk of transmitting viable viral-infected cells as well as viral infectivity in cell line culture | No growth of lesions                                                     |
| Dodhia (2018) [30] | Experimental study | 12 fibers   | Laryngeal papillomas     | Laser ablation         | KTP laser    | Ten fibers were sterilized in CIDEX for 12 min, whereas two fibers were left unsterilized. HPV DNA amplification with PCR HPV genotyping detection was done using type-specific probes and/or Sanger sequencing | Determine if HPV can be detected on a laser fiber after use, with or without sterilization | Over 27 strains of HPV were not detected on KTP fibers after use, with or without sterilization |
| Best (2020) [31]  | Experimental on animal model | 45          | Warts                    | Ablation of warts in the murine model with different technique | Scalpel vs KTP laser vs coblation | Nude laboratory mice with established MmuPV1 tail warts were treated with scalpel excision KTP laser ablation, and coblator treatment. Uninfected nude mice were challenged with surgical byproducts, including ablated and heated tissue, and surgical smoke products, surgical smoke collection, and analysis by PCR | Incidence and time course of the appearance of recurrent warts in mice | Rapid transmission of virus Byproducts of scalpel treatment: 50% penetrance of infection at day 13 and 100% at day 32. Byproducts of KTP laser: 50% by day 35 and 100% by day 52. Byproducts of coblation: 50% penetrance at day 59 and a maximum of 73% penetrance. Smoke plume captured during treatment with the KTP laser and coblator was highly infectious, as was the material captured in a laser filter |
### Table 2 (Continued)

| Reference          | Study design | Sample size | Disease            | Procedure                        | Energy                                                                 | Methods                                                                 | Endpoint                                                                 | Results                                                                 |
|--------------------|--------------|-------------|--------------------|-----------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Johnson (1991)     | Experimental | NA          | HIV                | Application of different energy to infected cells | Coagulation, cutting, router, bone saw, control                         | Cool vapors and aerosols produced by several common surgical power instruments and hot smoke plumes generated with electrocautery on known HIV-1 inoculated blood were gently bubbled through sterile viral culture media | HIV-1–positive cultured cells generated by the utilization of the 4 different surgical instruments | No infectious HIV-1 was detected in aerosols generated by electrocautery or with a manual wound irrigation. HIV-1 was cultured from cool aerosols and vapors generated by a 30 000 RPM spinning router tip, an instrument similar to the Midas Rex and the Stryker oscillating bone saw. |
| Hagen (1997)       | Experimental | 20          | Pseudorabies virus | Ablation of virus-infected tissue culture plate | Excimer laser                                                              | Infected tissue culture plates were laser treated in close proximity to uninfected plates | To test the possibility of pathogenic virus transmission into the operating suite during excimer laser treatment of corneal tissue. | None of the 20 uninfected plates was infected by the laser plume rising from the ablation of infected tissue culture plates. |
| Taravella (1997)   | Prospective  | 4           | Varicella-zoster virus | Ablation of fibroblasts infected with attenuated varicella-zoster virus | Excimer laser                                                              | PCR analysis and viral cultures were performed on the liquid in the trap. In addition, a Dacron swab, soaked in viral transport medium, was used on all ablations to test for virus in the silicone tubing used to collect the plume and the nearest ablated material. | Growth of varicella-zoster virus in cell cultures | No growth |
| Taravella (1999)   | Experimental | NA          | Oral polio virus   | Ablation of human embryonic lung fibroblast culture tissue | Excimer laser                                                              | Ablation plume was collected with suction provided by a laser smoke evacuation unit equipped with an LFS-103 filter. A bubble chamber was used to sample the plume. Ten milliliters of viral culture media were placed inside the trap. | Positive culture from inlet tube from the smoke evacuator and liquid from the bubble trap was also cultured | Live virus was shown in the material trapped from the laser plume. |

BPV = bovine papillomavirus; HIV = human immunodeficiency virus; HPV = human papillomavirus; NA = not available; NR = not reported; PCR = polymerase chain reaction.
whereas other failed to reproduce such findings [28,29]. However, in the most elegant animal model reported, Best et al [31] demonstrated recently the high transmissibility of the mouse papillomavirus (MmuPV1). Specifically, nude laboratory mice with established MmuPV1 tail warts were treated with scalpel excision, KTP laser ablation, and coblator treatment. Uninfected nude mice were subsequently challenged with surgical byproducts, including ablated and heated tissue, and surgical smoke products. Importantly, the study demonstrated extremely high penetrance of the infection in the mice exposed to all the different surgical byproducts (50% penetrance of infection at day 13 and 100% at day 32 with byproducts of scalpel treatment, 50% by day 35 and 100% by day 52 with byproducts of KTP laser, and 50% penetrance at day 59 and a maximum of 73% penetrance with byproducts of coablation). Similarly, the smoke plume captured during treatment with the KTP laser and coblator was also highly infectious, as was the material captured in a laser filter.

Concerning the studies investigating other viruses, cell cultures infected with different viruses (human immunodeficiency virus [HIV], pseudorabies virus, varicella-zoster virus, and oral poliovirus) have been treated with different lasers to identify the ability of the byproducts to generate infected positive cultured cells, mostly demonstrating negative results [32–35].

### 3.1.3. Risk of bias assessment

Supplementary Tables 1 and 2 summarize the risk of bias for clinical and preclinical studies, respectively.

Although virtually all the studies raised some concerns on potential biases in some of the domains of the NTP/OHAT Risk of Bias Rating Tool for Human and Animal Studies, the overall quality of most of the clinical and preclinical reports was good.

### 3.2. Discussion

COVID-19 pandemic is significantly modifying the health systems worldwide, with major implications also on the medical disciplines not primarily involved in the management of COVID-19 patients. Specifically, the vast majority of the centers in the areas more severely hit by the pandemic are limiting their surgical activities. Concerning surgery, a recent report from Zheng et al [6] highlighted the need to increase the awareness in the surgical community about the potential risks of virus diffusion due to aerosol dispersal during laparoscopic surgeries, known for several years, and several international surgical societies have called for caution or even discourage the use of a laparoscopic approach during the pandemic [7–11]. Based on these concerns, we elected to perform a systematic review of the literature to evaluate the real risk of virus diffusion through surgical smoke. We identified a significant number of clinical and preclinical research papers on the topic (Tables 1 and 2). In agreement with the purpose of the present review, the most robust evidence comes from the report of Kwak et al [27], where HBV DNA was demonstrated in the vast majority of the surgical smoke samples collected in 11 laparoscopic and robotic procedures. Most of the reports evaluated HPV virus and related disease, and the vast majority of the literature suggested a high risk of infection related to HPV.

Since the present systematic review adopted a standardized methodology to identify all the available evidence in the field, the present paper represents the ideal background to estimate the risk of diffusion of the novel SARS-CoV-2 virus for health professionals, for whom no clinical study is available. On the whole, although all the available data come from viruses that are very different from the novel coronavirus, considering that the SARS-CoV-2 virus has been shown in blood and stools [38,39], the theoretical risk of virus diffusion through surgical smoke cannot be excluded. Although specific clinical studies are needed to understand the effective presence of the virus in the surgical smoke of different surgical procedures and its concentration, adoption of all the required protective strategies seems mandatory. In this regard, all the measures suggested by Zheng et al [6] can be considered appropriate (eg, minimizing the use of electrocautery, reduction of pneumoperitoneum pressure, and generous use of suction devices to remove smoke and aerosol during operations, especially before converting from laparoscopy to open surgery or any extraperitoneal maneuver). On top of this, a preoperative nasopharyngeal sample for COVID-19 can be considered wise [40]. Having said that, the available pieces of evidence do not seem to be sufficient to recommend complete suspension of all the laparoscopic and robot-assisted surgical programs. This is clearly of value wherever the medical and economic resources available during this pandemic are sufficient to treat medical and surgical conditions other than COVID-19 patients.

The present study is not devoid of limitations. First, we were not able to identify any paper focused on the novel or other coronavirus, and most of the available studies were indeed focused on HPV, which is a very different kind of virus. This highlights the need for specific studies on the topic. Second, only a single study evaluated the presence of a virus in the smoke from laparoscopic procedures on patients infected with HBV [27]. The study assesses exactly the kind of surgical setting that is under discussion at present. Obliviously, viruses with large differences in structure may have different behavior in this regard, and the presence of a virus in the surgical smoke does not automatically imply an airborne contagion. However, some reports on HPV support such a possibility. Other studies are needed on SARS-CoV-2 and other viruses (eg, HBV, hepatitis C virus, and HIV) and other surgical procedures (eg, cholecystectomy, colectomy, radical prostatectomy, and radical hysterectomy, which are among the most frequently performed laparoscopic procedures worldwide). Moreover, it should also be considered that surgical smoke is also produced during open surgery. Li et al [41] recently reported on 30 open and laparoscopic surgical procedures in the obstetrics and gynecology operating rooms of three different hospitals from Taiwan, demonstrating that the cumulative number of particles of 0.3 and 0.5 μm in laparoscopic operation was higher than that in laparotomy after
10 min of using an electronic knife. However, the cumulative number of particles of 5 μm after 10 min of using the electronic knife was numerically higher in open cases. Although all the reported differences were not statistically significant, these warrant some caution also for open surgery, where surgical smoke evacuation and filtration should be better studied and implemented [42]. Third, although the present systematic review followed a strict methodology, the overall quality of the findings is mainly related to the quality of the available evidence. However, our assessment of the methodological quality of the reports through the NTP/OHAT Risk of Bias Rating Tool for Human and Animal Studies identified a large number of good methodological reports.

4. Conclusions

Although all the available data come from viruses that are very different from the novel coronavirus, considering that the SARS-CoV-2 virus has been shown in blood and stools, the theoretical risk of virus diffusion through surgical smoke cannot be excluded. Although specific clinical studies are needed to understand the effective presence of the virus in the surgical smoke of different surgical procedures and its concentration, adoption of all the required protective strategies, including preoperative patient nasopharyngeal swab for COVID-19, seems mandatory. The available pieces of evidence do not seem to be sufficient to recommend complete suspension of all the laparoscopic and robot-assisted surgical programs.

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Appendix A. Supplementary data

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