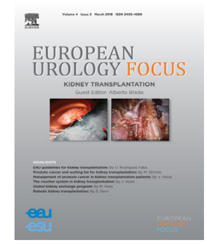
EUROPEAN UROLOGY FOCUS 6 (2020) 1058–1069

available at www.sciencedirect.com
journal homepage: www.europeanurology.com/eufocus



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

Nicola Pavan [a], Alessandro Crestani [b], Alberto Abrate [c], Cosimo De Nunzio [d], Francesco Esperto [e], Gianluca Giannarini [f], Antonio Galfano [g], Andrea Gregori [h], Giovanni Liguori [a], Riccardo Bartoletti [i], Francesco Porpiglia [j], Alchiede Simonato [c,k], Carlo Trombetta [a], Andrea Tubaro [d], Vincenzo Ficarra [l], Giacomo Novara [m,], on behalf of the Research Urology Network (RUN)*

[a] *Department of Urology, University of Trieste, Cattinara Hospital, Trieste, Italy;* [b] *Urology Unit, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy;* [c] *Urology Section, Department of Surgical, Oncological and Oral Sciences, University of Palermo, Palermo, Italy;* [d] *Department of Urology, Sant'Andrea Hospital, University La Sapienza, Rome, Italy;* [e] *Department of Urology, Campus Biomedico University of Rome, Rome, Italy;* [f] *Urology Unit, Academic Medical Centre Hospital 'Santa Maria della Misericordia', Udine, Italy;* [g] *Urology Unit, Niguarda Hospital, Milan, Italy;* [h] *Urology Unit, Ospedale Luigi Sacco, Milan, Italy;* [i] *Department of Translational Research and New Technologies, Urologic Unit, University of Pisa, Italy;* [j] *Division of Urology, Department of Oncology, School of Medicine, San Luigi Hospital, University of Turin, Orbassano, Italy;* [k] *Urology Unit, Department of Surgery, S. Croce e Carle Hospital, Cuneo, Italy;* [l] *Department of Human and Pediatric Pathology "Gaetano Barresi", Urologic Section, University of Messina, Messina, Italy;* [m] *Department Surgery, Oncology and Gastroenterology, Urologic Unit, University of Padova, Padova, Italy*

Article info

Article history:
Accepted May 29, 2020

Keywords:
Minimally invasive surgery
Virus
COVID-19
Surgical
smoke

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

* Corresponding author. Department of Surgery, Oncology, and Gastroenterology, Urology Clinic, University of Padua, Via Giustiniani 2 – 35100, Padua, Italy. Tel. 0039 049 8211250, Fax: 0039 049 8218757. (G. Novara).
E-mail addresses: giacomonovara@gmail.com, giacomo.novara@unipd.it (G. Novara).

https://doi.org/10.1016/j.euf.2020.05.021

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.

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,” “Orthognathic 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, Gloster 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, Lobraico et al [22] reported that the overall incidence of HPV-related lesions was 3.2% among laser surgeons treating verrucae with the CO_2 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

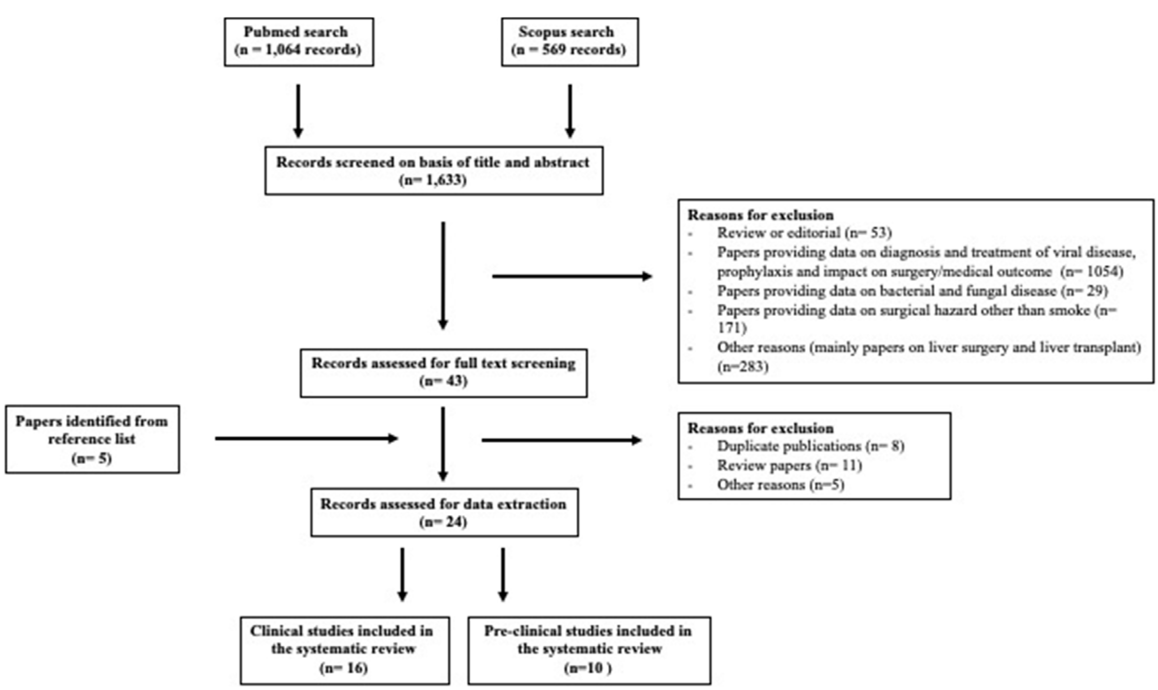


Fig. 1 – Flow diagram of the systematic review.

Table 1 – Clinical studies evaluating the risk of virus diffusion through surgical smoke.

Reference	Study design	Cases	Specialty	Disease	Surgery performed	Energy	Methods	Endpoint	Results
HPV									
Garden (1988) [36]	Prospective	7	Dermatology	Plantar or mosaic Verrucae	Ablation	CO_2 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 CO_2 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	CO_2 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	CO_2 laser	Collection of plumes and DNA extraction	To detect viral DNA in the plumes of smoke generated by CO_2 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	CO_2 laser	Collection of plumes and DNA extraction	To detect viral DNA in the plumes of smoke generated by CO_2 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	CO_2 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%)

Table 1 (*Continued*)

Reference	Study design	Cases	Specialty	Disease	Surgery performed	Energy	Methods	Endpoint	Results
Hallmo (1991) [17]	Case report	1	Otorhinolaryngology	Laryngeal papillomatosis	Removal from each vocal cord with a CO_2 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) [18]	Prospective	30	Dermatology	Genital warts	Genital warts	Electrocoagulation (n = 19) vs CO_2 laser (n = 11)	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) [19]	Retrospective comparative	31 surgeons vs 6124 patients	Dermatology	Warts in different sites	Laser vaporization	CO_2 laser	Clinical diagnosis in surgeons vs patients in population-based studies	Risks to surgeons of acquiring warts from the CO_2 laser plume vs risk of population	CO_2 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) [20]	Prospective	13	Plastic surgery	Aesthetic reasons	Laser resurfacing in the periorbital, perioral, or full-face regions	CO_2 laser (Tru-Pulse 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 CO_2 laser resurfacing Each of the 13 patients had one bacterial, one viral, and one control culture (total 39 specimens)	No viral growth
Hughes (1998) [21]	Prospective	5	Dermatology	Clinically typical verrucae vulgares of the extremities	Laser ablation	Erbium:YAG lase	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

Table 1 (*Continued*)

Reference	Study design	Cases	Specialty	Disease	Surgery performed	Energy	Methods	Endpoint	Results
Lobraico (1988) [22]	Retrospective	794	Multispecialty	HPV lesions	Laser ablation	CO_2 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 CO_2 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) [23]	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) [24]	Prospective	10	Otorhinolaryngology/ dermatology	Laryngeal papillomas and genital warts	Surgical removal and laser vaporization	CO_2 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) [25]	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 of high-grade squamous intraepithelial lesions of the cervix uteri might be contaminated with the DNA of high-risk HPV	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) [26]	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
Other viruses									
Kwak (2016) [27]	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.

Table 2 – Preclinical studies evaluating the risk of virus diffusion through surgical smoke.

Reference	Study design	Sample size	Disease	Procedure	Energy	Methods	Endpoint	Results
HPV								
Garden (1988) [36]	Prospective	4	Bovine papillomas	Ablation	CO_2 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 CO_2 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	CO_2 laser vs electrocoagulation	Collection of the smoke produced	The prepared extracts were assayed for infectious BPV by testing their ability to induce focal transformation of mouse c127 cells	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	CO_2 laser	Collection of the airborne particulate and culture	Southern blot testing of laser ejecta	Absence of viral organisms
		NR	Bovine papillomavirus	Ablation of lesion in dairy cattle mucosa in patients		Collection of the airborne particulate and inoculation in animals		No growth of lesions
Kunachak (1996) [29]	Prospective	10	Recurrent respiratory papillomatosis	Laser ablation	CO_2 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	Cell lines in the viral infectivity testing systems revealed no sign of viral infection
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
Other viruses								
Johnson (1991) [32]	Experimental study	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) [33]	Experimental study	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) [34]	Prospective	4	Varicella-zooster 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) [35]	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.

[36,37], 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 coblation). 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.

Author contributions: Nicola Pavan had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Pavan, Novara, Ficarra.
Acquisition of data: Pavan, Crestani, Abrate, De Nunzio, Esperto.
Analysis and interpretation of data: Novara, Giannarini, Galfano, Gregori.
Drafting of the manuscript: Novara, Pavan.
Critical revision of the manuscript for important intellectual content: Liguori, Bartoletti, Porpiglia, Simonato, Trombetta, Tubaro.
Statistical analysis: None.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: Liguori, Bartoletti, Porpiglia, Simonato, Trombetta, Tubaro.
Other: None.

Financial disclosures: Nicola Pavan certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

***Funding/Support and role of the sponsor*:** None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euf.2020.05.021.

References

[1] Centers for Disease Control and Prevention. Interim guidance for healthcare facilities: preparing for community transmission of COVID-19 in the United States. https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/guidance-hcf.html.
[2] American College of Surgeons. COVID-19: guidance for triage of non-emergent surgical procedures. https://www.facs.org/covid-19/clinical-guidance/triage.
[3] Royal College of Surgeons. COVID-19: good practice for surgeons and surgical teams. https://www.rcseng.ac.uk/standards-and-research/standards-and-guidance/good-practice-guides/coronavirus/.
[4] Stensland K.D., Morgan T.M., Moinzadeh A., et al. Considerations in the triage of urologic surgeries during the COVID-19 pandemic. Eur Urol. In press. https://doi.org/10.1016/j.eururo.2020.03.027.
[5] Ficarra V., Novara G., Abrate A., et al. Urology practice during COVID-19 pandemic. Minerva Urol Nefrol. In press. https://doi.org/10.23736/S0393-2249.20.03846-1.
[6] Zheng M.H., Boni L., Fingerhut A. Minimally invasive surgery and the novel coronavirus outbreak: lessons learned in China and Italy. Ann Surg. In press. https://doi.org/10.1097/SLA.0000000000003924.
[7] American College of Surgeons. COVID-19: considerations for optimum surgeon protection before, during, and after operation. https://www.facs.org/covid-19/clinical-guidance/surgeon-protection.
[8] SAGES and EAES. SAGES recommendation regarding surgical response to COVID-19 crisis. https://www.sages.org/recommendations-surgical-response-covid-19/.
[9] The Royal College of Surgeons of Edinburgh. Updated intercollegiate general surgery guidance on COVID-19. https://www.rcsed.ac.uk/news-public-affairs/news/2020/march/intercollegiate-general-surgery-guidance-on-covid-19-update.
[10] European Society for Gynaecological Endoscopy. Recommendations on gynaecological laparoscopic surgery during COVID-19 outbreak. https://esge.org/wp-content/uploads/2020/03/Covid19StatementESGE.pdf.
[11] EAU Robotic Urology Section. Guidelines during COVID-19 emergency. https://uroweb.org/wp-content/uploads/ERUS-guidelines-for-COVID-def.pdf.
[12] National Toxicology Program/Office of Health Assessment and Translation (NTP/OHAT). Risk of bias rating tool for human and animal studies. https://ntp.niehs.nih.gov/ntp/ohat/pubs/riskofbiastool_508.pdf.
[13] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009;151:264–9.
[14] Abramson AL, DiLorenzo TP, Steinberg BM. Is papillomavirus detectable in the plume of laser-treated laryngeal papilloma? Arch Otolaryngol Head Neck Surg 1990;116:604–7.
[15] Andre P, Orth G, Evenou P, Guillaume JC, Avril MF. Risk of papillomavirus infection in carbon dioxide laser treatment of genital lesions. J Am Acad Dermatol 1990;22:131–2.
[16] Ferenczy A, Bergeron C, Richart RM. Carbon dioxide laser energy disperses human papillomavirus deoxyribonucleic acid onto treatment fields. Am J Obstet Gynecol 1990;163(4 Pt 1):1271–4.
[17] Hallmo P, Naess O. Laryngeal papillomatosis with human papillomavirus DNA contracted by a laser surgeon. Eur Arch Otorhinolaryngol 1991;248:425–7.
[18] Bergbrant IM, Samuelsson L, Olofsson S, Jonassen F, Ricksten A. Polymerase chain reaction for monitoring human papillomavirus contamination of medical personnel during treatment of genital warts with CO_2 laser and electrocoagulation. Acta Derm Venereol 1994;74:393–5.

[19] Gloster Jr HM, Roenigk RK. Risk of acquiring human papillomavirus from the plume produced by the carbon dioxide laser in the treatment of warts. J Am Acad Dermatol 1995;32:436–41.
[20] Capizzi PJ, Clay RP, Battey MJ. Microbiologic activity in laser resurfacing plume and debris. Lasers Surg Med 1998;23:172–4.
[21] Hughes PS, Hughes AP. Absence of human papillomavirus DNA in the plume of erbium:YAG laser–treated warts. J Am Acad Dermatol 1998;38:426–8.
[22] Lobraico RV, Schifano MJ, Brader KR. A retrospective study on the hazards of the carbon dioxide laser plume. J Laser Appl 1988;1:1–8.
[23] Calero L, Brusis T. Laryngeal papillomatosis—first recognition in Germany as an occupational disease in an operating room nurse [article in German]. Laryngorhinootologie 2003;82:790–3.
[24] Ilmarinen T, Auvinen E, Hiltunen-Back E, Ranki A, Aaltonen Lm, Pitkäranta A. Transmission of human papillomavirus DNA from patient to surgical masks, gloves and oral mucosa of medical personnel during treatment of laryngeal papillomas and genital warts. Eur Arch Otorhinolaryngol 2012;269:2367–71.
[25] Neumann K, Cavalar M, Rody A, Friemert L, Beyer DA. Is surgical plume developing during routine LEEPs contaminated with high-risk HPV? A pilot series of experiments. Arch Gynecol Obstet 2018;297:421–4.
[26] Zhou Q, Hu X, Zhou J, Zhao M, Zhu X, Zhu X. Human papillomavirus DNA in surgical smoke during cervical loop electrosurgical excision procedures and its impact on the surgeon. Cancer Manage Res 2019;11:3643–54.
[27] Kwak HD, Kim SH, Seo YS, Song KJ. Detecting hepatitis B virus in surgical smoke emitted during laparoscopic surgery. Occup Environ Med 2016;73:857–63.
[28] Wisniewski PM, Warhol MJ, Rando RF, Sedlacek TV, Kemp JE, Fisher JC. Studies on the transmission of viral disease via the CO2 laser plume and ejecta. J Reprod Med 1990;35:1117–23.
[29] Kunachak S, Sithisarn P, Kulapaditharom B. Are laryngeal papilloma virus-infected cells viable in the plume derived from a continuous mode carbon dioxide laser, and are they infectious? A preliminary report on one laser mode. J Laryngol Otol 1996;110:1031–3.
[30] Dodhia S, Baxter PC, Ye F, Pitman MJ. Investigation of the presence of HPV on KTP laser fibers following KTP laser treatment of papilloma. Laryngoscope 2018;128:926–8.
[31] Best SR, Esquivel D, Mellinger-Pilgrim R, Roden RBS, Pitman MJ. Infectivity of murine papillomavirus in the surgical byproducts of treated tail warts. Laryngoscope 2020;130:712–7.
[32] Johnson GK, Robinson WS. Human immunodeficiency virus-1 (HIV-1) in the vapors of surgical power instruments. J Med Virol 1991;33:47–50.
[33] Hagen KB, Kettering JD, Aprecio RM, Beltran F, Maloney RK. Lack of virus transmission by the excimer laser plume. Am J Ophthalmol 1997;124:206–11.
[34] Taravella MJ, Weinberg A, Blackburn P, May M. Do intact viral particles survive excimer laser ablation? Arch Ophthalmol 1997;115:1028–30.
[35] Taravella MJ, Weinberg A, May M, Stepp P. Live virus survives excimer laser ablation. Ophthalmology 1999;106:1498–9.
[36] Garden JM, O'Banion MK, Shelnitz LS, et al. Papillomavirus in the vapor of carbon dioxide laser-treated verrucae. JAMA 1988;259:1199–202.
[37] Sawchuk WS, Weber PJ, Lowy DR, Dzubow LM. Infectious papillomavirus in the vapor of warts treated with carbon dioxide laser or electrocoagulation: detection and protection. J Am Acad Dermatol 1989;21:41–9.
[38] Chang L., Yan Y., Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfus Med Rev. In press. https://doi.org/10.1016/j.tmrv.2020.02.003.
[39] Zhang W, Du RH Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect 2020;9:386–9.
[40] Simonato A., Giannarini G., Abrate A., et al. Pathways for urology patients during the COVID-19 pandemic. Minerva Urol Nefrol. In press. https://doi.org/10.23736/S0393-2249.20.03861-8.
[41] Li CI, Pai JY, Chen CH. Characterization of smoke generated during the use of surgical knife in laparotomy surgeries. J Air Waste Manag Assoc 2020;70:324–32.
[42] Limchantra IV, Fong Y, Melstrom KA. Surgical smoke exposure in operating room personnel: a review. JAMA Surg 2019;154:960–7.