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Review

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Could Laparoscopic Concerns During Coronavirus Pandemic Affect the Care of Women With Pregnancy of Unknown Location/Ectopic Pregnancy?

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Abstract

In the coronavirus pandemic elective surgery has been deferred and therefore emergency surgery for suspected ectopic pregnancy arises as the most commonly performed operation in gynecology. Laparoscopic management has traditionally been the gold standard, however recently concerns have been raised regarding severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) dissemination as aerosolized small particles are presumed to escape abdominal cavity. The rationale for this hypothesis is based on cohort studies confirming presence of blood-borne viruses such as human immunodeficiency virus (HIV) and hepatitis B virus (HBV) in the surgical plume, whereas data for airborne viruses such as SARS-CoV-2 are scarce. Remarkably, there is no solid evidence up to date to associate inhalation of pneumoperitoneum viral particles with subsequent disease of theatre staff. Reverse transcription-polymerase chain reaction (RT-PCR) on blood samples of coronavirus disease 2019 (COVID-19)-infected patients presenting with fever, confirmed viremia in only 1% of cases. The viral ribonucleic acid (RNA) was isolated in stool samples in 29% of cases but was not found in urine samples. Therefore, the use of surgical energy devices on genital tract tissues bears little chance of producing aerosolized COVID-19 particles. The optimal surgical approach should be individualized according to a variety of factors: complexity of case and bowel involvement, length of procedure, comorbidities, hospital stay, as well as the surgeon's familiarity with each approach. When necessary precautions are taken, laparoscopy for ectopic pregnancy appears safe. Operating theatres should meet technical specifications and maintain negative pressure if possible. Only essential personnel equipped with personal protective equipment should be attending theatres. Abdominal pressure should be set under 12 mm Hg and ultrasonic/bipolar device use minimized. Smoke evacuation filtration systems and disposable trocars with insufflation taps can contain surgical smoke. As more information is emerging, trusts will adjust to evolving circumstances with standard operating procedures. Changing established practice may be premature as clinicians should "first do no harm".

Keywords: Coronavirus; Laparoscopy; Ectopic pregnancy

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Introduction

It has recently been reported that 20% of health care workers in Italy have been infected by coronavirus, which understandably has created anxiety among the scientific community [1]. We have now seen at least 180 doctors and nurses dying in the UK. Undoubtedly, access to appropriate personal protective equipment (PPE) remains the cornerstone of the problem.

Among other key issues, concerns have been raised regarding the risk of severe acute respiratory syndrome (SARS) that might be caused due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) dissemination during minimally invasive surgery. Pneumoperitoneum-related aerosolized small particles containing the virus ribonucleic acid (RNA) are presumed to escape from the abdominal cavity, due to pressure difference, and can subsequently be inhaled by theatre staff. Steps of particular relevance include retrieval of surgical specimens, as well as the final desufflation of the abdominal cavity. Small particles are also likely to escape around the port sites or through the trocars when inserting and removing laparoscopic instruments. Obviously, this possibility is directly proportional to the abdominal pressure maintained throughout the procedure as well as the complexity and length of each case.

However, during the coronavirus disease 2019 (COVID-19) pandemic, all elective surgeries have been deferred, with the exception of suspected cancer cases. This policy was introduced in an effort to minimize the spread of the virus, but also in order to increase availability of staff and equipment, e.g., ventilators, intensive care unit (ICU) beds. In regard to emergency gynecological surgery, surgical management of incomplete miscarriage has been largely substituted by manual vacuum aspiration (MVA). Consequently, emergency surgery for suspected/confirmed ectopic pregnancy, which is traditionally laparoscopic, may currently be the most commonly performed operation in gynecology.

Evidence of Viruses/Bacteria Presence in Pneumoperitoneum

The rationale of the hypothesis of coronavirus aerosolization during laparoscopy was based on studies on blood-borne viruses, such as hepatitis B virus (HBV) and human immunodeficiency virus (HIV). In 2016, a Korean study proved the existence of HBV in surgical smoke in 10 out of 11 patients undergoing laparoscopic colorectal procedures [2]. HIV-1 can remain viable in cool aerosols generated by certain surgical power tools that raises the possibility of HIV transmission to medical personnel exposed to aerosols, similarly, generated during the care of HIV-infected patients [3].

An outbreak of group A *Streptococcus* (GAS) has been reported in a hospital, after highlighting two cases that underwent uncomplicated laparoscopic surgery in the same operating room [4]. GAS is a traditional skin-to-skin/mucosa-to-mucosa transmitted pathogen. None of the 46 members of the staff that came in contact with these patients were found to be colonized with the same strain of GAS. Infection control investigation concluded that aerosolization of particles from the first patient was the most possible source of transmission, despite the lack of definite evidence.

It is crucial to highlight that there are limited data regarding classical airborne infections. There are case reports of port sites tuberculosis following laparoscopy. However, they were associated with poor disinfection between theatre cases, as none of the patients exhibited clinical signs of tuberculosis perioperatively [5]. Bioaerosol produced at low temperature as in harmonic scissors may contain live multidrug resistant *Mycobacterium tuberculosis* [6].

Evaporation/Sublimation of Infected Tissues is not Unique for Laparoscopy

Notably, the fact that production of surgical smoke constitutes an occupational health hazard has not come as a surprise to the scientific community [7]. The inhalation of airborne particles has not only been associated with transmission of infections, but also with upper respiratory tract irritation and possible carcinogenesis. Surgical smoke is produced by the use of energy devices and as such, it is not unique for laparoscopic surgery. In fact, as experienced surgeons argue, better containment and filtration of the surgical gas and plume can be achieved by laparoscopy compared to laparotomy, as a closed system can be designed [8].

Human papillomavirus (HPV) deoxyribonucleic acid (DNA) has been found in surgical smoke in 29.9% of cases undergoing cervical loop electrosurgical excision procedures (LEEP). The positive rate of HPV DNA in surgical smoke was significantly increased for greater distances of the suction device from the surgical site. Flow fluorescence in situ hybridization on nasal epithelial cells of the surgeons detected HPV DNA in 1.5% of them (2 out of 134). After a 3 - 6-month follow-up, the nasal swabs from these two doctors tested negative for HPV DNA [9]. Greater amounts of HPV DNA were usually recovered in the laser vapor (carbon dioxide (CO_2)) compared to the electrocoagulation vapor produced during treatment of human plantar warts [10].

Poliovirus, which is classified as airborne virus, has been detected in the smoke produced by ablation of infected fibroblasts using excimer laser [11].

Electrosurgery generates the smallest particles with a mean diameter of 0.07 µm, laser-generated particles are typically larger up to 0.31 µm, while the ultrasonic scalpel by-products are the largest, with particle diameters ranging from 0.35 to 6.5 µm [12]. Traditional surgical masks are able to capture particles greater than 5 µm and as such they offer no protection against particles produced by electrosurgical and laser devices. Therefore, systems for continuous smoke evacuation have been implemented [13].

Taken together, it can be deduced that the sole advantage of open surgery, in terms of preventing transmission of a virus during a pandemic, lies in the ability to minimize or completely avoid the use of any energy devices. This needs to be balanced against the standard risks of open surgery, such as needle stick injury [14] and contact with other bodily fluids, as well as the impact on the patient due to longer hospital stay. A summary of relevant studies is displayed in Table 1 [2-6, 9-11, 15].

Can Coronavirus Be Found in Blood, Abdominal Tissues or Bodily Fluids? Can It Be Transmitted Through Contact With These Tissues? Does It Exist in the Pneumoperitoneum?

It needs to be stressed that up to date there is no study to report presence of coronavirus RNA in pneumoperitoneum of infected patients. But even if presence was to be confirmed in the future, it wouldn't necessarily mean that it can cause clinical infection as it may not be in sufficient amount or appropriate form.

Interestingly, reverse transcription-polymerase chain reaction (RT-PCR) on blood samples of COVID-19-infected patients presenting with fever, confirmed viremia in only 1% of cases. Furthermore, as expected for an airborne virus that can be swallowed and carried through the gastrointestinal tract, it was present in stool samples in 29% of cases. Coronavirus RNA was not detected in any of the urine samples taken from 72 patients [16]. Vertical transmission of SARS-CoV-2 has not been detected, although perinatal transmission was suspected in one case [17]. Thus, the theoretical risk of presence of coronavirus particles in the pneumoperitoneum of patients undergoing gynecological surgery, appears to be negligible, except for cases where bowel is involved.

SARS-CoV-2 is an RNA virus that has a size range of 0.06 to 0.14 µm [18]. All respiratory viruses normally attach to receptors in the airways (with the exception of adenoviruses) and therefore the feasibility of blood-borne transmission of respiratory viruses is unlikely. At this point, it should be highlighted that no transmissions by blood or other substances of human origin have been documented or alleged for novel coronavirus (2019-nCoV). Interestingly, this is in consistency with data for the other two coronaviruses that have emerged over the past two decades (SARS-CoV and MERS-CoV, causing Mideast respiratory syndrome) [19].

Table 1. Summary of Available Studies Regarding Presence of Bacteria/Viruses in Surgical Smoke and Transmission of Relevant Infections

Studies	Findings
Laparoscopy	
Blood-borne	
Kwak et al, 2016 [2]	HBV detected in surgical smoke, n = 10 out of 11
Airborne	
Ramesh et al, 2003 [5]	Tuberculosis, n = 8
Al-ajmi et al, 2012 [4]	GAS, n = 2 out of 46
Chowdhury et al, 2011 [6]	*Mycobacterium tuberculosis*, viral DNA of HBV, HCV, HIV and HPV in surgical smoke
Open procedures	
Blood-borne	
Johnson et al, 1991 [3]	HIV blood samples
Zhou et al, 2019 [9]	HPV PCR, 29.9% of n = 134
Sawchuk et al, 1989 [10]	HPV PCR, 5 out of 8 lasers, 4 out of 7 electrocoagulation processes
Airborne	
Chowdhury et al, 2011 [6]	*Mycobacterium tuberculosis*, viral DNA of HBV, HCV, HIV and HPV
Others	
Capizzi et al, 1998 [15]	*Staphylococcus*, *Corynebacterium*, *Neisseria*, n = 13
Taravella et al, 1999 [11]	Poliovirus

HBV: hepatitis B virus; GAS: group A *Streptococcus*; DNA: deoxyribonucleic acid; HCV: hepatitis C virus; HIV: human immunodeficiency virus; HPV: human papillomavirus; PCR: polymerase chain reaction.

Management of Patients in Need of Emergency Laparoscopic Surgery Should Be Individualized

While the surgical approach remains controversial for the scientific community, it becomes apparent that management of the patients should be individualized. Coronavirus status could possibly be taken into consideration, whenever available, but the sensitivity of a single PCR swab (nasal/throat) does not exceed 63%. However, as the influx of coronavirus patients is increasing, every emergency case has to be treated as positive, until proven otherwise. Symptoms and contact questionnaires may be more relevant for the triage of semi- elective cases operated under the green pathway.

Most scientific societies addressed the concerns, assessed evolving evidence and released joint statements that endorsed laparoscopic approach, at least for procedures that do not involve the bowel [20]. In an effort to focus on surgical exposure, anesthetic considerations are commonly underemphasized, even though airway manipulation is the classical aerosol generating process. Intubation and extubation of the patient are by far the riskiest interventions and therefore spinal anesthesia may be an alternative for gynecological laparotomies or certain minimally invasive cases, e.g., hysteroscopies, large loop excision of the transformation zone (LLETZ) and surgical evacuation of products of conception.

Thus, the most essential parameter to acknowledge may be the type of surgery as well as the surgeon's expertise that will affect the exposure time. In the specific case of suspected or confirmed ectopic pregnancy the patient is offered diagnostic laparoscopy ± unilateral salpingectomy/salpingotomy. Most commonly, this is a very quick procedure with minimal use of electrosurgical devices, which can even be performed using low abdominal pressure (under 12 mm Hg). In the rare cases of technically difficult procedure due to unexpected findings, e.g., abdominal adhesions, cesarean scar/interstitial/cornual pregnancy, laparoscopy is typically abandoned and converted to laparotomy.

Coronavirus Pandemic-Associated Dilemmas in the Management of Symptomatic Women With Pregnancy of Unknown Location/Suspected Ectopic Pregnancy

The management of pregnancy of unknown location/ ectopic pregnancy has been established by high quality papers. However, there are specific groups of patients that may be affected by coronavirus associated concerns and the possible reluctancy of clinicians to proceed with intervention. Indeed, a recent observational study from a university hospital in Bologna found that the rate of ruptured ectopic pregnancies in the coronavirus pandemic lockdown increased significantly [21].

Symptomatic patients presenting with severe abdominal pain and bleeding would normally be offered a diagnostic laparoscopy when scan findings are inconclusive. Depending on the unit, up to 30% of these patients will not have

an ectopic pregnancy [22], which poses a clinical dilemma that becomes even greater under the current circumstances. On one hand, open procedure would be debatable with these high rates of negative findings, especially when we take into account that the patient will have to undergo an unnecessary hospital stay during coronavirus pandemic. On the other hand, missing the diagnosis of an ectopic pregnancy can have detrimental effects caused by rupture of the ectopic pregnancy and hemorrhagic shock. Some of these patients will be subjected to long hospital stay due to uncertainty regarding optimal management.

Anyhow, systematic reviews of case series of pregnant women undergoing surgical procedures in pregnancy have shown that laparotomy and laparoscopy are both safe and have similar obstetric outcomes. An increased ratio of fetal loss after laparoscopy has been attributed to its preferential use in early pregnancy, when the possibility of miscarriage is higher [23].

In another group of patients, the ones with minor symptoms and pregnancy of uncertain viability with scan findings favoring ectopic pregnancy, a diagnostic laparoscopic procedure +/- treatment of ectopic pregnancy or conservative follow up would be offered, according to patient's preferences, set clinical criteria, e.g., blood human chorionic gonadotropin (hCG) levels, presence of free peritoneal fluid and inert characteristics, e.g., language barrier, committed to follow up patient. In the coronavirus pandemic, when by definition there is a need to reduce hospital attendances and unnecessary semi-elective interventions, methotrexate administration appears tempting. It is a mild immunosuppressive medication, but it is unlikely to cause vulnerability to COVID-19 at the dose used to treat ectopic pregnancy and it does not require shielding [24]. However, as doctors we should "first do no harm" and have zero tolerance for mistakenly diagnosing miscarriage, or ectopic pregnancy in cases where very early and viable intrauterine pregnancy exists [25]. In this sense, methotrexate should be strictly reserved for cases of persistent pregnancy of unknown location after excluding viability or in cases where an ectopic pregnancy that fulfils criteria for medical management is confirmed. We propose the algorithm depicted in Figure 1 for the management of suspected ectopic pregnancy during the coronavirus pandemic.

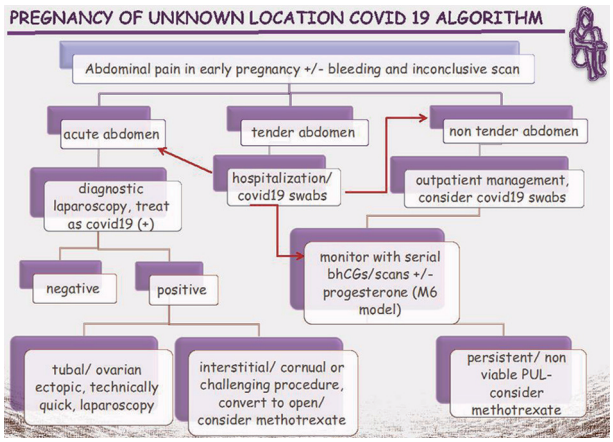

Figure 1. Proposed algorithm for the management of PUL during COVID-19 pandemic. COVID-19: coronavirus disease 2019; PUL: pregnancy of unknown location; bhCG: blood human chorionic gonadotropin.

Safety Precautions During Laparoscopy

There is a fine balance between safety of all theatre staff and safety of the patient. Local protocols fitted to population characteristics and staff expertise may be relevant and should be encouraged. Regardless of the chosen approach, all necessary precautions should be in place to reduce the chance of exposure. Operating theatres should meet technical specifications; ideally, they could be converted to negative pressure rooms, so that airborne contaminants are contained within the room. This offers optimal protection to staff working in adjacent areas [26]. It can be achieved with the incorporation of a much stronger low-level exhaust system, which leads to a downward extraction of air. The vertical airflow stream is presumed to make infectious particles flow below the operating table until being drawn out of the room via the exhaust grilles. This means that surgical staff are at little risk of being infected by the patient during the operation. Heating, ventilation, air-conditioning (HVAC) systems perform multiple functions simultaneously, including controlling at least three known central variables in the airborne transmission of infectious particles: temperature, relative humidity and air currents. With regard to ventilation, various international scientific organizations, including Centers for Disease Control and Prevention (CDC), recommend a minimum of 15 - 20 air exchanges per hour, 3 - 4 (20%) of which must be fresh air [27]. Only essential personnel should be attending theatres and they should all be equipped with appropriate PPE. When available, a closed smoke evacuation/filtration system with ultra-low particulate air (ULPA) filtration capability should be employed. Skin incisions should be small, and trocars ideally have insufflation tap, so as to eliminate leakage of CO_2 through port sites. Serving the same rationale, instrument diameter should fit the trocar, e.g., don't use 5-mm camera through 12-mm trocar. Electrosurgical and ultrasonic scalpels should be used with caution and in a manner that minimizes production of plume, with low power setting and avoidance of long desiccation times. A trocar's one-way valve is recommended to be attached to suction's tube through filters in order to remove surgical plume during use of energy to prevent blurred imaging. Specimens should be retrieved in endobag following active desufflation of pneumoperitoneum with closed smoke evacuation/filtration system or laparoscopic suction. This practice will also diminish blood/fluid droplet spray or spread [28].

Conclusions

It appears necessary to adapt laparoscopic practice to the evolving circumstances as the coronavirus may be part of the everyday life possibly for the next few months if not years. As more information is emerging, our understanding of the virus biology will shed light to the optimal care for surgical emergencies. Until then, changing established management may be

premature reaction and therefore international societies have not altered their published recommendation algorithms on ectopic pregnancy during coronavirus pandemic. Medical treatment remains the standard of care and surgical intervention should be undertaken when clinically indicated.

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None to declare.

Conflict of Interest

None to declare.

Author Contributions

Sofia F. Makrydima perceived the idea, edited and reviewed the manuscript. Dorothea Saragli edited and reviewed the manuscript.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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