Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

NEW METHODS

Visualizing endoscopy-generated aerosols with laser light scattering (with videos)

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Background and Aims: Upper GI endoscopy is speculated to be an aerosol-generating procedure (AGP). Robust evidence exists for aerosol transmission of severe acute respiratory syndrome coronavirus 2. The quality of data available confirming aerosol generation during GI endoscopy is limited. We aimed to objectively demonstrate that GI endoscopy is an AGP and illustrate the mechanism by which the greatest risk for aerosolization of droplets during endoscopy may occur.

Methods: Aerosolized droplets generated during insertion and withdrawal of an endoscope and with passage of various tools through the endoscopic working channel using 2 experimental apparatuses modeling an upper GI tract (ie, a fluid-filled tube and a lamb esophagus) were qualitatively assessed by laser light scattering.

Results: Insertion and withdrawal of the upper endoscope into the upper GI tract models generated numerous aerosolized particles. A large number of brightly scattering particles were observed at the site of insertion and withdrawal of the endoscope. Passage of a cytology brush, biopsy forceps, and hemostatic clip through the working endoscope channel also generated aerosolized particles but in fewer numbers. There was no significant variation in quantity or brightness of droplets generated on testing different biopsy valve cap models or when suctioning fluid with an open versus closed biopsy valve cap. These results were reproducible over several trials.

Conclusions: We illustrate in an objective manner that upper GI endoscopy is an AGP. These findings may have implications for transmission of infectious airborne pathogens outside of severe acute respiratory syndrome coronavirus 2 and can help to inform guidance on appropriate personal protective equipment use and other measures for transmission risk mitigation during GI endoscopy.

Robust evidence exists for the possibility of both aerosol and fomite transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which can remain viable and infectious in aerosols and on surfaces for hours.[1] Of particular concern to healthcare workers are aerosol-generating procedures (AGPs).[2] Upper GI endoscopy is believed to be among those AGPs that pose increased risk for airborne transmission. The novel SARS-CoV-2 virus enters into host cells via cell receptor angiotensin-converting enzyme II and the transmembrane serine protease 2, both of which are highly expressed in the GI tract. Consequently, infected patients who sneeze, cough, or retch during the procedure can produce a large number of virus-laden aerosol particles. At present, however, no

Abbreviations: AGP, aerosol-generating procedure; COVID-19, coronavirus disease 2019; HEPA, high-efficiency particulate air; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

DISCLOSURE: *All authors disclosed no financial relationships. Research support for this study was provided by the intramural research program of the National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health.*

DIVERSITY, EQUITY, AND INCLUSION: One or more of the authors of this paper self-identifies as an under-represented gender minority in science. While citing references scientifically relevant for this work, we actively worked to promote gender balance in our reference list.

0016-5107/$36.00
https://doi.org/10.1016/j.gie.2022.07.030

Received March 30, 2022. Accepted July 26, 2022.

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scientific studies have confirmed SARS-CoV-2 transmission through the aerosol route during GI endoscopy, and the quality of data available is very low and limited to a single prospective study.[3] Given the paucity of data and substantial disagreement as to whether GI endoscopies are in fact AGPs, the GI community has found itself grappling with the potential aerosolization risk of endoscopic procedures without the benefit of quantitative evidence to guide best practices.[2] This dilemma is becoming ever more apparent as clinicians and hospitals face challenging decisions on how to safely resume elective procedures with vaccination of the general population well underway.

The aim of this study was to evaluate whether GI endoscopy procedures are capable of generating potentially infectious aerosols in the absence of sneezing, coughing, or retching. During GI endoscopy, the endoscope is inserted into and withdrawn from a fluid-lined tract, and in both diagnostic and therapeutic GI endoscopy, endoscopic tools pass bidirectionally through a working channel of the endoscope. During these procedures, the surfaces of these tools become coated with secretions and fluids from the upper respiratory and GI tracts. We developed a laser light–scattering setup capable of visualizing airborne particles and used this apparatus to assess whether these procedures are capable of generating aerosols from fluids that wet these tools and can therefore contribute to airborne transmission of disease.

METHODS

Laser-scattering setup

Two separate laser-scattering setups were used in this study. As shown in Figure 1, a vertically oriented laser light sheet (green, 527 nm) was used to visualize droplets generated when inserting and withdrawing tools through the biopsy valve cap on the handle of the endoscope. The endoscope was inserted into a U-shaped plastic tube that was partially filled with an aqueous solution containing 2% glycerol, and its terminus was positioned near the bottom of the U-tube. The surfaces of tools inserted into the endoscope channel became wetted with the glycerol–water solution. Droplets generated at the interface between the biopsy valve cap on the handle and the inserted tools were directed toward the light sheet by high-efficiency particulate air (HEPA)-filtered air blowing gently through a nozzle. Flashes of light were readily observed when droplets passed through the light sheet. The 2% glycerol additive simulates the nonvolatile content in oropharyngeal and gastric fluids and without which smaller droplets could fully evaporate before passing through the light sheet and thereby avoid detection.

As shown in Figure 2, a horizontally oriented light sheet was used to visualize droplets generated when inserting and withdrawing the endoscope through a lamb esophagus.

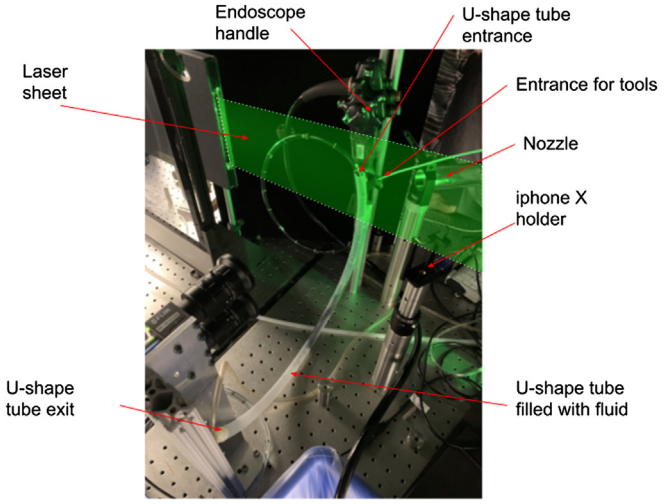

Figure 1. Laser-scattering setup with U-tube. A 4-inch-tall vertical laser light sheet (green, 527 nm) was centered 12 inches above the table (*semi-transparent green trapezoid* indicates the location of the laser sheet) and offset approximately 2 inches from the biopsy valve cap on the endoscope handle. The endoscope handle was strapped securely to a pair of vertically orientated aluminum rods. The entrance to the U-shaped plastic tube and the biopsy valve cap on the endoscope handle were both positioned approximately 12 inches above the table. The U-shaped tube was partially filled with an aqueous solution containing 2% glycerol. High-efficiency particulate air was directed through a nozzle toward the biopsy valve cap on the endoscope handle, which helped propel particles generated in that vicinity toward the light sheet for visualization. Two types of cameras were used to record video of the light scattering events: an iPhone camera secured on a support viewed the light sheet at a low scattering angle and afforded a qualitative assessment of the particle production (camera not shown), and 2 side-by-side 12-megapixel monochrome complementary metal-oxide semiconductor (CMOS) cameras provided higher resolution video of the scattering events.

Both setups were located below HEPA filters whose downward laminar airflow excluded contamination from airborne dust particles in the room air. Aerosolized particles generated on insertion or removal of the endoscope from the lamb esophagus or when inserting and withdrawing tools from the working channel of the endoscope produced flashes of light as they passed through a nearby laser light sheet. The light-scattering events were recorded by an iPhone camera (Apple, Cupertino, Calif, USA), which afforded a qualitative assessment of the particle production, and 2 side-by-side scientific-grade cameras that provided higher resolution video of the scattering events. The recorded video footage was analyzed to qualitatively assess the generation of aerosols.

Endoscope and tools

This study used a standard upper GI endoscope (GIF-HQ190; Olympus, Center Valley, Pa, USA) and 3 commonly used endoscopic tools: a biopsy forceps (Radial Jaw 4 large capacity with needle, 2.8-mm single use biopsy forceps; Boston Scientific, El Coyol, Alajuela, Costa Rica), cytology brush (Infinity cytology brush; Steris, Mentor, Ohio, USA),

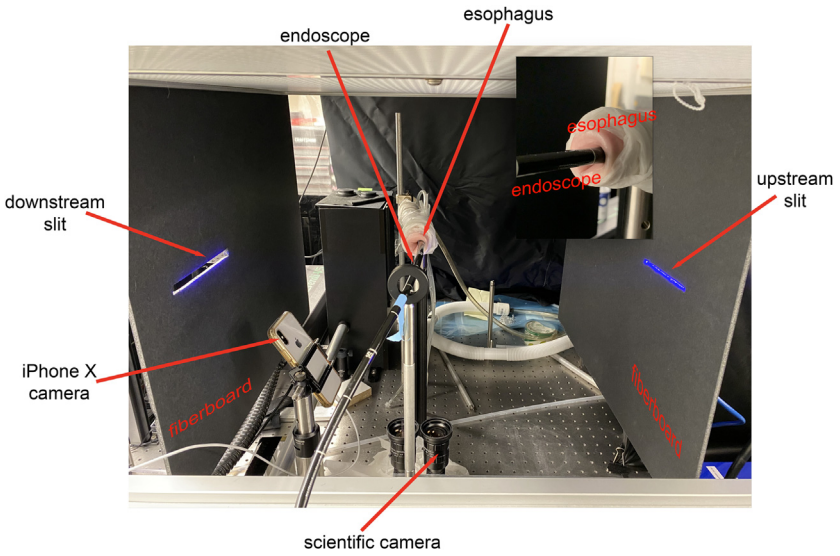

Figure 2. Laser-scattering setup with lamb esophagus. A 100-mm wide horizontal laser light sheet (blue, 447 nm) was positioned 17.5 inches above the optical table. Fiberboard barriers were secured on 2 sides of a 2 × 4-foot high-efficiency particulate air filter to reduce boundary flow effects. Slits cut into the barriers past the laser light sheet. The lamb esophagus was inserted inside a wetted flexible polyethylene tube (1 and 1/8 inch inner diameter × 1 foot long Bilge and Pump Hose; Everbilt, Atlanta, Ga, USA), folded back over either end of the tube, and the folded portions wrapped with dampened paper towels. Humidified nitrogen was flowed through the esophagus to keep the esophageal tissue from drying out and to simulate airflow that occurs out of the esophagus during a routine upper GI endoscopy. Particles produced when withdrawing the endoscope from the esophagus generated flashes of light as they fell through the light sheet. Two types of cameras were used to record video of the light-scattering events: an iPhone camera positioned below and downstream of the lamb esophagus afforded a qualitative assessment of the droplets, and 2 side-by-side upward-looking 12-megapixel monochrome CMOS cameras provided higher resolution video of the scattering events.

and hemostatic clip (QuickClip Pro, single-use repositionable clip; Olympus). Additionally, 2 separate biopsy valve caps made from different materials were tested. The endoscope instruments were inserted and withdrawn through the biopsy valve cap using the same speed and technique applied during a standard upper endoscopy procedure. Each endoscopic instrument was inserted and withdrawn several times to ensure repeatability.

RESULTS

Lamb esophagus

Repeated insertion and withdrawal of the upper endoscope through the horizontally supported lamb esophagus generated aerosolized particles (Video 1, available online at www.giejournal.org) whose number appeared to be proportional to the speed at which the endoscope was inserted and withdrawn. A thin film of fluid between the endoscope and lamb esophagus surfaces could be visualized forming and rupturing during displacement of the endoscope (Videos 2a and 2b, available online at www.giejournal.org), which appears to be the principal source of the aerosolized particles.

Biopsy valve caps

Repeated insertion and withdrawal of 3 different endoscopic instruments (biopsy forceps, hemostatic clip, and cytology brush) into 2 different endoscopic biopsy valve caps were evaluated. The BioShield biopsy valve (Steris) is made of rubber and has a pre-existing perforation to facilitate penetration of endoscopic instruments, whereas the Complete Disposable Valve Set–Biopsy Valve (Olympus) is made of silicone rubber and lacks a pre-existing perforation in the cap. Insertion of dry instruments through dry biopsy valve caps did not generate aerosolized droplets, as expected. However, once the tool and its shaft became wetted, repeated insertion and withdrawal of endoscopic instruments through the biopsy valve caps generated aerosolized particles. No marked difference was seen in the quantity of particles generated as the shaft of the endoscopic instruments passed bidirectionally through either model of biopsy valve cap; however, their number appeared to increase with increasing speed at which the endoscope was inserted and withdrawn. Significant differences were observed when the wetted tool at the end of the shaft was pulled through the biopsy valve cap. Withdrawal of the biopsy forceps generally produced a greater number of aerosolized particles as the head of the closed forceps passed through the biopsy valve cap (Video 3, available online at www.giejournal.org). Withdrawal of the hemostatic clip generated similar results (Video 4, available online at www.giejournal.org). A wetted cytology brush that was not properly retracted inside the shaft generated the greatest quantity of aerosolized particles when pulled through the biopsy valve (Video 5 [available online at www.giejournal.org], Fig. 3). Finally, no

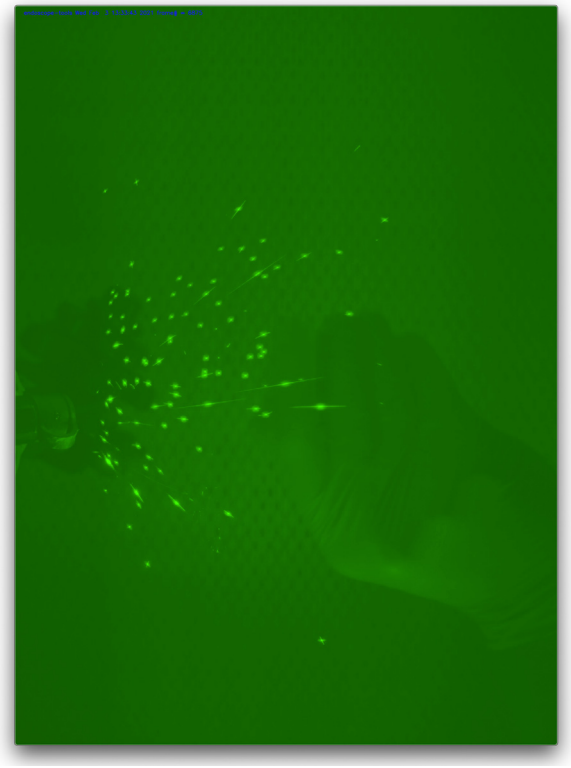

Figure 3. Representation of endoscopy-generated aerosolization of particles caused by wetted cytology brush withdrawn from biopsy valve of endoscope (using cylindrical tubing model).

significant variation in quantity or brightness of droplets generated on suctioning of fluid with an open versus closed biopsy valve cap occurred.

DISCUSSION

At present, there are no objective reports of SARS-CoV-2 transmission through endoscopy. In this study, using models to simulate standard upper GI endoscopic procedures, we demonstrated that upper endoscopy is capable of generating aerosolized droplets. Although there has been a theoretical concern for potential aerosol generation, prior studies have not systematically assessed which procedures are capable of aerosol generation during endoscopy or the mechanism by which aerosolization may occur. Here, we provide visual evidence of endoscopy-generated droplets and qualitatively describe possible mechanisms by which droplets can be aerosolized during a standard endoscopic procedure.

Video recordings confirmed that aerosolized particles can be generated when the upper endoscope is inserted into and withdrawn from a lamb esophagus whose luminal diameter, esophageal tissue composition, and distensibility are similar to a human esophagus. Video recordings also confirmed that all 3 endoscopic instruments, when wetted, generate aerosolized droplets during bidirectional passage through the biopsy valve caps.

Fluids wetting adjacent surfaces merge when coming into contact, and on separation, the liquid film that forms between those surfaces can rupture and generate small droplets that are invisible to the naked eye. This mechanism of droplet generation applies to both insertion and withdrawal of an endoscope and insertion and withdrawal of endoscopic tools through the biopsy valve cap. Droplets generated during insertion and withdrawal of the endoscope can be expelled out of the oral cavity by pressurized air injected through the endoscope or exhaled air from the patient. When endoscopic tools are inserted into and withdrawn from the biopsy valve cap, the soft cap material scrapes most of the liquid from the shaft surface, but bidirectional passage of the shaft through the cap causes the material to periodically stretch and snap back, with any liquid present at the interface being launched in the form of small droplets. We did not observe any marked difference in aerosolized particles generated with the 2 different models of biopsy valve cap. Significantly, when the cytology brush is inadvertently extended from the shaft during withdrawal, its bristles are folded inward as they pass through the biopsy valve cap and snap back when emerging on the other side, generating a comparatively large number of droplets.

Of particular concern are droplets <100 μm in size, which shrink as their 95% to 99% aqueous fraction fully evaporates, forming aerosolized particles that can linger in the air for minutes and can be transported over large distances by air currents. The risk of exposure to aerosolized oropharyngeal and GI secretions is of paramount importance to endoscopists and other personnel present during intervention of the upper GI tract, particularly because most procedures are done in non-negative pressure rooms. The risk of exposure is not only to the endoscopist performing the maneuver but also the endoscopy technician or nurse and any other personnel in the procedure room, including anesthesia staff.

In this study, we opted to assess particular endoscopic tools because they are frequently used for diagnostic and therapeutic purposes during routine upper GI endoscopy. Specifically, cytology brushing is used in cases where an infectious disease is being assessed. Our findings could be extrapolated to potential exposure to other infectious pathogens that could be aerosolized with use of cytology brushing. Similarly, hemostatic clips are frequently used for therapeutic purposes in cases of GI bleeding. In this same manner, there is potential for exposure to aerosolization of bloodborne pathogens on withdrawal of a contaminated hemostatic clip. As such, the findings of this study have implications for transmission of infectious airborne pathogens outside of SARS-CoV-2 and could help to better inform clinical guidelines on appropriate personal protective equipment (PPE) use for routine upper GI endoscopy outside of those performed during pandemics.

In the context of the emerging pandemic and because of concern over possible exposure to the SARS-COV-2 virus during GI endoscopy, the American Gastroenterology Association published a rapid recommendation document in April 2020 with the aim of providing evidence-based, clinical guidance addressing PPE recommendations for GI endoscopy. Because of limited studies providing direct evidence to inform clinical questions for PPE in coronavirus disease 2019 (COVID-19), data were predominantly drawn from experience during the SARS outbreak.[4] Aside from assuming that the mode of SARS-COV-2 transmission is comparable with that of the SARS virus without confirmatory evidence, these studies were further limited by inclusion of a small cohort size and use of data on tracheal intubation or bronchoscopy rather than data from GI endoscopy, with the assumption that the risk of aerosolization during endoscopy is equivalent to that during bronchoscopy, despite a lack of objective data to support this theory. In this manner, our study adds considerably to the existing literature by providing visual evidence for the mechanism by which aerosolization can occur specific to GI endoscopic procedures, helping to inform appropriate PPE needed during endoscopy.

The SARS-CoV-2 global pandemic continues to place worldwide health systems under unprecedented pressure with ongoing community transmission from asymptomatic individuals and the emergence of novel SARS-COV-2 variants.[5-7] Several factors place endoscopy staff at a uniquely increased risk of acquiring SARS-COV-2. Endoscopy suites tend to be closed units with several attending people including endoscopists, nursing staff, technicians, anesthetists, and patients. The endoscopists accesses the GI lumen from a close distance and therefore can potentially be exposed to a large number of respiratory, oropharyngeal, and GI flora.[8] This theory is supported by a study conducted in 2019 that demonstrated a significant unrecognized exposure to the endoscopist's face of potentially infectious biologic samples during endoscopy, along with unrecognized contamination on the walls of endoscopy suites.[9] SARS-CoV-2 has been detected in gastric, duodenal, and rectal biopsy samples, which represent potential sources of infection in endoscopy settings.[10] Additionally, coughing, sneezing, and retching can occur during upper endoscopy, which are known to generate aerosols. These expulsions are of particular concern, because the size distribution and volume of droplets emitted per liter of air expelled are orders of magnitude greater than that generated during normal exhalation in a healthy person at rest ($\leq$15 fL/L). Although most of the liquid volume generated falls to the ground rather quickly, a large number of smaller droplets will dehydrate before falling to the ground and remain airborne for minutes; therefore, all personnel in the procedure room may be at risk for potential exposure. Furthermore, routine maneuvers done while performing endoscopy, including suctioning and multiple exchanges of catheters and instruments through the potentially contaminated endoscope, increase the risk of splashing and spread of infective material to the endoscopy staff.

Although this is the first study to visualize aerosolization of particles during a simulated routine upper GI endoscopy procedure, 2 important limitations are worth noting. First, the experiments were limited to a small number of endoscopic equipment. The endoscopic instruments selected for this demonstration were based on the premise that their texture and composition would influence particle generation because of friction on passage through the working channel of the endoscope. Although we may have inadvertently introduced a selection bias, the similarity of results obtained with the endoscopic instruments and biopsy valve caps tested suggests that droplet generation is to be expected as these tools pass bidirectionally through the valve caps. Second, the qualitative nature of our study limits the scope of what can be inferred. As compared with prior studies, we did not use a particle counter to quantitatively characterize the particle size distribution or assess the relative role aerosols may play in the transmission of viruses.[11] Nevertheless, gauze pad–assisted instrument withdrawal of tools through the biopsy valve cap may prove effective at mitigating the risk of fluid aerosolization during this procedure. Our aim was to provide visual evidence of endoscopy-generated droplets and to qualitatively describe the means by which aerosolization may occur during a routine endoscopy. We propose that quantifying particle generation during GI endoscopy should be the subject of future studies on this topic; such studies may help to accurately assess the effectiveness of interventions proposed to lower the risk of infection from aerosol particles generated during endoscopic procedures.

In conclusion, since the inception of this global pandemic, health policy pertaining to COVID-19 has largely shifted away from an initial strategy of containment to mitigation. In light of PPE supply chain shortages[12] and the potential for false-negative preprocedure COVID-19 screening tests,[13] the question of whether GI endoscopy qualifies as an AGP and can lead to nosocomial transmission is thus of paramount importance. During the pandemic, measures used by endoscopy facilities to prevent exposure during GI endoscopy led to workflow disruptions, mainly with regard to lengthy procedure room turnover times, reductions in procedure capacity, and worsened staff working conditions (ie, implementing new safety protocols, reprocessing facilities, donning and doffing PPE, etc), despite a lack of evidenced-based analysis of the potential for airborne transmission during GI endoscopy.[14] By visualizing endoscopy-generated droplet aerosols, our study helps identify procedures that pose the greatest risk for aerosolization during standard GI endoscopy. These findings can help

better inform clinical guidelines on appropriate PPE and other measures for transmission risk mitigation during GI endoscopy while allowing healthcare workers to continue to deliver safe and efficient care.

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