Introduction
Since the onset of the Coronavirus Disease 2019 (COVID-19) pandemic, the risks of aerosol-generating procedures (AGPs) as the COVID-19 transmission route is of universal concern among health care personnel [1]. Under experimental circumstances, SARS-CoV-2 has exhibited aerosol transmission and remains viable and infectious up to 3 hours [2]. Currently, a growing body of published evidence points towards endoscopic procedures being considered as aerosol-generating [3, 4].
tion to esophagastroduodenoscopy (EGD), endoscopic retrograde cholangiopancreatography (ERCP) [5] and colono-
scopic procedures have a risk of infection, considering the re-
cent detection of the SARS-CoV-2 in specimens and feces [6–
8]. Contaminated droplets and aerosols originate mainly from
the patients’ upper or lower gastrointestinal tract and previous
reports have mainly focused on preventing the spread of these
aerosols [9,10].

However, contaminated aerosolization emanating directly
from the flexible endoscope device (e.g. air/water, suction and
biopsy valves) or endoscopic tools have not been explored [11,12]. The aim of this study was to investigate if use of endo-
scopic tools during flexible endoscopy may permit gas leakage
from the scope or tools. Specifically, we investigated areas
within the endoscope handle and endoscope tool (as these
areas are close to the operators’ and assistants’ faces during a
procedure).

Material and methods

Ex-vivo setting

In an ex-vivo model using a 35-cm fresh porcine rectum seg-
ment, an endoscope (PCF-H180AL, Olympus) was inserted
from the distal end of the rectum, and the manometer (Nosh-
ok) was placed inside of the proximal end to measure the in-
traluminal pressure near the endoscope tip (Supplementary
Fig. 1). Both sides of the intestine were tightened using tie
bands and rubber bands to create a closed system.

Leakage from the biopsy valve

A semi-disposable (#MB-358, Olympus) or disposable (Orca-
Pod, Boston Scientific) biopsy valve were sequentially attached
to the endoscope. The endoscope handle was placed in a water
bath and completely submerged to test for the presence of gas
leakage. Ten trials, confirmed by the presence or absence of
bubble formation, were performed under three different condi-
tions:
1. No endoscopic device was placed inside the biopsy channel.
2. Each of 10 endoscopic devices was inserted into and re-
moved from the biopsy valve.
3. Each endoscopic device was inserted into the biopsy channel
and its insertion angle was changed manually.

The intestine was then inflated up to 74.7 mmHg (40 inH\textsubscript{2}O) or
until gas leakage from the biopsy valve was detected, using the
inflation button on the endoscope to pump air into the intesti-
te. The average time to reach 74.7 mmHg was 10 seconds.
The shaft of devices was clamped to prevent the gas leakage
from the device handles. We chose 74.7 mmHg as the highest
pressure limit as higher pressures will tear mucosa and muscle
wall of the fresh pig colon in our experience.

Leakage from endoscopic tools

Endoscopic tools during the study included: two biopsy forceps
(Single-Use Radial Jaw [Boston Scientific] and Single-Use Radial
Jaw Hot [Boston Scientific]); two endoscopic clips (DuraClip
[ConMed] and Resolution Clip [Boston Scientific]); three endo-
scopic snares (Singular Polypectomy Snare [ConMed], Captiva-
tor Single-Use Snare [Boston Scientific] and SnareMaster
[Olympus]); three endoscopic submucosal dissection (ESD) kni-
ves (DualKnife [Olympus], DualKnife J [Olympus] and Flush
Knife [Fujifilm]) were investigated in this study. Endoscopic
snares, endoscopic knives, and Resolution Clip, which has the
jaw inside the over-sheath when inserting into the biopsy chan-
nel, were termed devices without an exposed jaw. Other devi-
ces (biopsy forces and DuraClip\textsuperscript{TM}) were termed devices with
an exposed jaw.

Each endoscopic device was inserted into the biopsy channel
whilst the entire endoscope handle was submerged in the water
bath. The intestine was slowly inflated up to 74.7 mmHg (40
inH\textsubscript{2}O) 10 times or until gas leakage was detected. We used
semi-disposable biopsy valves for this experiment and con-
firmned no gas leakage from the biopsy valve.

Outcomes measurements

Videos were recorded during all the experiments. The primary
outcome measurement was the visible presence of gas bubbles
emanating from the biopsy valve or the device handle. Second-
ary outcome measurements included the leak pressure and the
amount of gas leakage. Instantaneous or continuous gas leak-
age was quantified as below.

Instantaneous gas leakage from the biopsy valve upon the
insertion of each endoscopic device was evaluated by using the
change in intraluminal pressure from the initial pressure
(18.7 mmHg [10 inH\textsubscript{2}O]). A pressure of 18.7 mmHg is com-
monly achieved during endoscopic insufflation to distend the bowel
wall. Continuous gas leakage from the biopsy valve by changing
the insertion angle (from 0 to 30 degrees) of devices or from the
device handles was evaluated. The required time for the in-
traluminal pressure to drop from 18.7 to 0 mmHg was meas-
ured, which was termed the required time\textsubscript{18.7 to 0 mmHg}. The test-
ing was terminated if it took longer than 90 seconds.

Statistical analysis

Differences in continuous variables between groups were evalu-
ated by the Mann-Whitney U test. The association between
two non-continuous parameters was evaluated by the Fisher
exact test. All analyses were performed using SPSS for Windows
v.10 (SPSS, Chicago, IL). \(P < 0.05\) was considered as significant.

Results

Gas leakage from the biopsy valve

Without tool insertion

No gas leakage as confirmed with lack of bubbles was ob-
erserved from semi-disposable or disposable biopsy valves up to
74.7 mmHg (40 inH\textsubscript{2}O) without endoscopic device inser-
tion.

Upon inserting and removing endoscopic tools

Gas leakage, as confirmed with presence of bubbles, was always
present upon insertion and removal of the biopsy forceps and
DuraClip (exposed jaw tools) at 0 mmHg (60/60 trials, 100%,
but infrequently with other devices (e.g., Resolution Clip, endoscopic snares, and ESD knives) (17/140 trials, 12.1%, Table 1). However, these devices had a higher frequency of gas leakage at even 1.9 mmHg (1 inH₂O) (95/140 trials, 67.9%).

To measure the extent of instantaneous gas leakage, the drop in intraluminal pressure upon insertion and removal of each device at 18.7 mmHg (10 inH₂O) was measured. The drop in pressure was significantly greater in using devices with an exposed jaw than other devices (8.4 ± 2.0 vs 2.3 ± 1.1 mmHg, P < 0.001, Fig. 1b). When analyzed via semi-disposable and disposable biopsy valve groups, 5 out of 10 devices had significantly higher gas leakage from the semi-disposable biopsy valve than from the disposable one (Supplementary Table 1).

Regarding DuraClip, which has an area of metal coil shaft which is uncovered with a polyethylene outer sheath near its tip, there was gas leakage from this area (Fig. 1c).

Table 1  Gas leakage from the biopsy valve upon insertion and removal of endoscopic tools.

| Endoscopic device | Gas leakage at 0mmHg | Gas leakage at 1.9 mmHg (1 inH₂O) |
|-------------------|----------------------|----------------------------------|
|                   | Semi- Disposable     | Semi- Disposable                 |
| Biopsy forceps    | Single-Use Radial Jaw 10/10 (100%) | 10/10 (100%) |
|                   | Single-Use Radial Jaw Hot 10/10 (100%) | 10/10 (100%) |
| Endoscopic clip   | DuraClip              | 1/10 (10%) 7/10 (70%) |
|                   | Resolution Clip¹     | 1/10 (10%) 2/10 (20%) |
| Endoscopic snare  | Singular Polypectomy Snare 0/10 | 0/10 |
|                   | Captivator Single-Use Snare 0/10 | 0/10 |
|                   | SnareMaster           | 5/10 (50%) 10/10 (100%) |
| ESD knife         | DualKnife             | 2/10 (20%) 10/10 (100%) |
|                   | DualKnife J²          | 0/10 |
|                   | FlushKnife²           | 0/10 |

Semi-, semi-disposable biopsy valve; Disposable, disposable biopsy valve; ESD, endoscopic submucosal dissection.

¹ This device has a jaw inside its over-sheath.
² Injectable ESD knife.
Gas leakage from the biopsy valve upon insertion angle alteration

After tip insertion, as each endoscopic device was passed until it protruded from the tip of the endoscope, there was no gas leakage from the semi-disposable biopsy valve. However, a continuous gas leakage was confirmed from the disposable biopsy valve in inserting ESD knives (DualKnife and DualKnife J), whilst no gas leakage in inserting other devices (Fig. 2a).

Gas leakage occurred from the biopsy valve whilst the insertion angle of each endoscopic device was changed manually from zero degrees to approximately 30 degrees of angulation (Fig. 2b and Supplementary Table 2). The required time 18.7 to 0 mmHg was significantly shorter in using endoscopic snares and ESD knives than biopsy forceps and endoscopic clips (snare vs ESD knives vs forceps vs clips = 33.5 ± 6.0 vs 28.3 ± 8.3 vs 41.2 ± 10.0 vs 68.3 ± 25.3 sec, Fig. 2c). Divided into semi-disposable and disposable biopsy valve groups, 5 out of 10 endoscopic devices had significantly shorter required time 18.7 to 0 mmHg in using the disposable biopsy valve than in using the semi-disposable one (Supplementary Table 2).

Gas leakage from endoscopic device handles

Each endoscopic device handle was submerged whilst inserted into the endoscope biopsy channel. Eight of 10 devices had a continuous gas leakage from their handles at low intraluminal pressures, particularly endoscopic snares (0 mmHg) and Flush Knife (0.7 ± 0.8 mmHg) (Fig. 3a and Table 2). As for these three devices, two endoscopic snares had similar

Fig. 2 Gas leakage from the biopsy valve while inserting endoscopic tools all the way. a Gas leakage from the disposable biopsy valve without changing the insertion angle of ESD knife (red arrow: bubble formation). b Before (left) and after (right) changing the insertion angle of biopsy forceps (red arrow: bubble formation). c The required time 18.7 to 0 mmHg while changing the insertion angle of endoscopic devices was evaluated. Each dot indicates each trial (black dot: semi-disposable biopsy valve, red dot: disposable biopsy valve). Bars indicate the mean ± SD. †: No gas leakage was noted, and the testing was terminated in 90 seconds (N = 12). * P < 0.005, ** P < 0.001.

Fig. 3 Gas leakage from endoscopic device handles. a Gas leakage from the handle of an endoscopic snare (red arrowhead). b Injectable ESD knife with a three-way stopcock connected to the water jet cap (red arrowhead).
time, 8.7 to 0 mmHg, of handle gas leakage as compared to gas leakage from the biopsy valve while changing the insertion angle (Supplementary Table 2 and Table 2).

For two injectable ESD knives, there was gas leakage from the water jet cap. However, connecting a 3-way stopcock onto the cap prevented gas leakage when exchanging syringes for submucosal injection (Fig. 3b).

Discussion

In the present study, to our knowledge we have presented for the first time the presence of significant gas leakage from the biopsy valve upon insertion and removal of endoscopic tools. In addition, we have shown that the alteration of the endoscopic tool insertion angle through the biopsy channel affects the degree of gas leakage. Moreover, continuous gas leakage was noted from the endoscope tool handles as well as a clear disparity in leakage between disposable and semi-disposable biopsy valves.

Bronchoscopy is known as a common AGP and likely presents a high potential risk of COVID-19 transmission to healthcare workers [1, 13, 14]. Besides the high exposure to bronchoscopists, the bioaerosol concentrations in bronchoscopy units also increases during procedures [15]. The same risk should be considered during upper endoscopy, which causes the patient to cough and mechanically create and disperse aerosols [3, 4].

A prospective study demonstrated unrecognized exposure of contaminated splash to the endoscopist’s face, and also individuals standing up to 6 feet away from the patients during the endoscopy [16]. Our results indicated one of the causes might be the gas leakage from the biopsy valve or endoscopic device handles, an alarming finding considering the short distance from the endoscopy teams’ faces.

Given there was no gas leakage from the biopsy valve without endoscopic device insertion, screening endoscopy alone (without biopsy or intervention) could be relatively safe in terms of the exposure to gas leakage from the biopsy valve. During the COVID-19 outbreak, most elective and non-urgent endoscopy has been postponed or canceled, whilst emergency (e.g. acute gastrointestinal bleeding, obstructions, and acute cholangitis) or time-sensitive endoscopy (e.g. cancer) has continued. These latter procedures require the frequent use of various endoscopic tools [3, 17–20]. These urgent procedures will continue to be required, for potentially COVID-19 positive patients or untested patients due to the lack of time prior to the procedure, thus our data seems extremely important during this time period.

The amount of gas leakage from the biopsy valve varied depending on the devices in this study. Upon inserting and removing endoscopic tools, the shape of the device tip (with or without an exposed jaw) was the main factor. Moreover, the devices with smaller diameter had more gas leakage. On the other hand, while we changed the insertion angle of endoscopic tools, the softer device shafts caused more gas leakage in addition to the smaller diameter.

Interestingly, semi-disposable biopsy valves had less gas leakage whilst we changed the insertion angle of endoscopic tools, but more gas leakage upon inserting and removing tools. Generally, semi-disposable biopsy valves are more durable to keep their shape compared with disposable biopsy valves. On the other hand, the insertabilty of semi-disposable valves is a little worse, which might lead to taking more time to insert and remove endoscopic tools in semi-disposable valves. We believe that these are the reasons for the difference in the amount of gas leakage happened between these valves.

| Table 2 | Gas leakage from endoscopic device handles. |
|---|---|
| Endoscopic device | Gas leakage at 74.7 mmHg (40 inH₂O) | Leak pressure (mmHg) | Required time 8.7 to 0 mmHg (sec) |
| Biopsy Forceps | Single-Use Radial Jaw | 10/10 (100 %) | 16.8 ± 2.5 | 90¹ |
| | Single-Use Radial Jaw Hot | 0/10 (0 %) | No leak | No leak |
| Endoscopic Clip | DuraClip | 10/10 (100 %) | 11.6 ± 1.1 | 90¹ |
| | Resolution Clip² | 0/10 (0 %) | No leak | No leak |
| Endoscopic Snare | Singular polypectomy snare | 10/10 (100 %) | 0 | 31 ± 4.4 |
| | Captivator single-use snare | 10/10 (100 %) | 0 | 28.3 ± 2.6 |
| | SnareMaster | 10/10 (100 %) | 7.9 ± 1.7 | 90¹ |
| ESD Knife | DualKnife | 10/10 (100 %) | 13.9 ± 2.7 | 90¹ |
| | DualKnife J³ | 10/10 (100 %) | 7.9 ± 1.7⁴ | 90¹ |
| | FlushKnife³ | 10/10 (100 %) | 0.7 ± 0.8⁴ | 79.8 ± 3.9 |

ESD: endoscopic submucosal dissection.
¹ The testing was terminated when it took longer than 90 seconds.
² This device has a jaw inside its over-sheath.
³ Injectable ESD knife.
⁴ Three-way stopcock was connected to the injection fluid cap of Injectable ESD knife.
Our study highlights special concerns during ESD procedures: maximal leakage was noted whilst changing the insertion angle of ESD knives and upon insertion and removal of forceps. ESD procedures require the long-time use of ESD knives and frequent insertion and removal to exchange other therapeutic devices, such as hemostasis forceps. In addition, ESD procedures can produce more electrocautery smoke, with viable cellular material that subsequently has a risk of infection [21].

Continuous gas leakage was noted more frequently from the disposable biopsy valve compared to the semi-disposable valve, and this should be considered when choosing which equipment to use.

Gas leakage from endoscopic device handles was a surprise observation during our study. This was observed from most tools as a steady leak and with the proximity of these tool handles to the endoscopists’ and assistants’ faces was a cause for concern.

Based on the results of this study, we recommend the following:

1. Insert and remove endoscopic devices from the biopsy valve quickly under a low intraluminal pressure.
2. Keep the devices vertical (at a straight angle) to the biopsy valve.
3. Consider use of semi-disposable biopsy valve, and
4. Place some kind of protective shield between the valve and the endoscopist and assistant who may be holding the device handle.

Based on our study as well, we suggest that the biopsy valve and endoscopic device handles be kept as far away as possible from the faces of endoscopy personnel.

The use of personal protective equipment (PPE) in performing AGPs is recommended by all societies in this COVID-19 pandemic era [3, 22, 23]. It is unknown how much amount of aerosol exposure is related to the risk of infection of endoscopy personnel with PPE. Based on these recommendations, most of the endoscopy personnel use PPE which includes a respirator (e.g. N95, FFP2, or equivalent), gown, gloves, eye protection, and apron, focusing on aerosols from the patients. However, our study suggests that endoscopy personnel also need to pay attention to the risk of possible COVID-19 transmission near the faces and length of the therapeutic procedures, the potential risks of this gas leakage, which could contribute to aerosolization, should not be neglected. In the short term, effective technical and protection strategies should be developed to minimize risk. In the long term, endoscopic and endoscopic tool design changes should be considered to minimize the risk of pathogenic contamination.

Conclusion

In summary, gas leakage from the biopsy valve and device handles commonly occur during endoscopic procedures where tools must be inserted in and out of the biopsy valve. Due to the proximity of these tools to the endoscopists’ and assistants’ faces and length of the therapeutic procedures, the potential risks of this gas leakage, which could contribute to aerosolization, should not be neglected. In the short term, effective technical and protection strategies should be employed to minimize risk.

Acknowledgments

The authors thank Yuko Tonohira for her assistance during the conduct of this study.

Competing interests

The authors declare that they have no conflict of interest.

References

[1] Judson SD, Munster VJ. Nosocomial transmission of emerging viruses via aerosol-generating medical procedures. Viruses 2019; 11: 940
[2] van-Deremalen N, Bushmaker T, Morris DH et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med 2020; 382: 1564–1567
[3] Soetikno R, Teoh AY, Kaltenbach T et al. Considerations in performing endoscopy during the COVID-19 pandemic. Gastrointest Endosc 2020; 92: 176–183
[4] Repici A, Maselli R, Colombo M et al. Coronavirus (COVID-19) outbreak: what the department of endoscopy should know. Gastrointest Endosc 2020; 92: 192–197
[5] An P, Huang X, Wan X et al. ERCP during the pandemic of COVID-19 in Wuhan, China. Gastrointest Endosc 2020; 92: 448–454
[6] Wu D, Wu T, Liu Q et al. The SARS-CoV-2 outbreak: What we know. Int J Infect Dis 2020; 94: 44–48

[7] Xiao F, Tang M, Zheng X et al. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology 2020; 158: 1831–1833

[8] Gu J, Han B, Wang J. COVID-19: Gastrointestinal manifestations and potential fecal-oral transmission. Gastroenterology 2020; 158: 1518–1519

[9] Marchese M, Capannolo A, Lombardi L et al. Use of a modified ventilation mask to avoid aerosolizing spread of droplets for short endoscopic procedures during Coronavirus Covid-19 outbreak. Gastrointest Endosc 2020; 92: 439–440

[10] Neven L, Sanja SS, Lucija VJ et al. Plexiglass barrier box to improve ERCP safety during the COVID-19 pandemic. Gastrointest Endosc 2020; 92: 428–429

[11] Mele A, Spada E, Sagliocca L et al. Risk of parenterally transmitted hepatitis following exposure to surgery or other invasive procedures results from the hepatitis surveillance system in Italy. J Hepatol 2001; 35: 284–289

[12] Kovaleva J, Peters FT, van der Meij HC et al. Transmission of infection by flexible gastrointestinal endoscopy and bronchoscopy. Clin Microbiol Rev 2013; 26: 231–254

[13] Zietsman M, Phan LT, Jones RM. Potential for occupational exposures to pathogens during bronchoscopy procedures. J Occup Environ Hyg 2019; 16: 707–716

[14] Lentz RJ, Colt H. Summarizing societal guidelines regarding bronchoscopy during the COVID-19 pandemic. Respirology 2020; 25: 574–577

[15] Lavoie J, Marchand G, Cloutier Y et al. Evaluation of bioaerosol exposures during hospital bronchoscopy examinations. Environment Sci Proc Impacts 2015; 17: 288–299

[16] Johnston ER, Habib-Bein N, Dueker JM et al. Risk of bacterial exposure to the endoscopist’s face during endoscopy. Gastrointest Endosc 2019; 89: 818–824

[17] Zhang Y, Zhang X, Liu L et al. Suggestions of infection prevention and control in digestive endoscopy during current 2019-nCoV pneumonia outbreak in Wuhan, Hubei province, China. Endoscopy 2020; 52: 312–314

[18] Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol 2012; 107: 345–360

[19] Cavaliere K, Levine C, Wander P et al. Management of upper Gl bleeding in patients with COVID-19 pneumonia. Gastrointest Endosc 2020; 92: 454–455

[20] Ehiken H, Schachtsch G, Mann O et al. Waiting times for endotherapy of early malignancy: No problem? Gastrointest Endosc 2020; 92: 424–426

[21] Alp E, Bijl D, Bleichrodt RP et al. Surgical smoke and infection control. J Hosp Infect 2006; 62: 1–5

[22] Castro Filho EC, Castro R, Fernandes FF et al. Gastrointestinal endoscopy during COVID-19 pandemic: an updated review of guidelines and statements from international and national societies. Gastrointest Endosc 2020; 92: 440–445

[23] World Health Organization. Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19): Interim Guidance, 19. 2020: Available from: https://apps.who.int/iris/handle/10665/331215

[24] Chen JH, Yu Y, Yang Z et al. Intraluminal pressure patterns in the human colon assessed by high-resolution manometry. Sci Rep 2017; 7: 41436

[25] Hirota M, Miyazaki Y, Takahashi T et al. Dynamic article: steady pressure CO2 colonoscopy; its feasibility and underlying mechanism. Dis Colon Rectum 2014; 57: 1120–1128

[26] Kato M, Nakajima K, Yamada T et al. Esophageal submucosal dissection under steady pressure automatically controlled endoscopy (SPACE): a clinical feasibility study. Endoscopy 2014; 46: 680–684

[27] Mukai S, Itoi T, Baron TH et al. Indications and techniques of biliary drainage for acute cholangitis in updated Tokyo Guidelines 2018. J Hepatobiliary Pancreat Sci 2017; 24: 537–549

[28] Mintz Y, Arezzo A, Boni L et al. A low cost, safe and effective method for smoke evacuation in laparoscopic surgery for suspected coronavirus patients. Ann Surg 2020; 272: 7–8