ported increased ICG uptake in surrounding tissues, such as the thyroid, thymus, and lymph nodes,[5] making the findings of 2 ectopic parathyroid glands in the thymus tissue by Kennedy et al[1] promising for this technique.

The advancements made by the authors in the identification of ectopic parathyroid glands may be a result of incremental improvements in NIR imaging devices or the experience of this team with optimal ICG dosing and imaging window. Various groups have shown that these components influence imaging performance across various tumor types and intraoperative imaging agents.[6] While these parameters must be determined for each tumor type and imaging agent, Kennedy et al[1] provide the foundation for integration of ICG-based imaging into endocrine surgery. Another consideration of using NIR imaging agents is their limited tissue penetration depth, which is both wavelength and tissue type dependent. Future studies may benefit from using molecules in the second NIR window (1000-1400 nm) with greater tissue penetration depths or using other optical contrast agents that are specific for parathyroid tissue to yield better sensitivity or specificity. We and others have demonstrated the use of targeted antibody-fluorophore conjugates in the NIR range,[7] and similar approaches may aid in differentiating parathyroid glands from surrounding tissues.

The study findings from Kennedy et al[1] demonstrate the benefit of ICG-based fluorescence vs parathyroid autofluorescence. Given the high SBR, safety, and timing window of ICG imaging, larger studies should be performed to identify occult or ectopic parathyroid glands in the operating room.

Marisa E. Hom, PhD
Eben L. Rosenthal, MD

Author Affiliations: Department of Otolaryngology–Head and Neck Surgery, Stanford University School of Medicine, Stanford, California.

Corresponding Author: Eben L. Rosenthal, MD, Department of Otolaryngology–Head and Neck Surgery, Stanford University School of Medicine, 875 Blake Wilbur Dr, Stanford, CA 94305 (elr@stanford.edu).

Published Online: May 6, 2021. doi:10.1001/jamaoto.2021.0628

Conflict of Interest Disclosures: None reported.

1. Kennedy GT, Azari FS, Newton AD, et al. Use of near-infrared molecular imaging for localizing visually occult parathyroid glands in ectopic locations. *JAMA Otolaryngol Head Neck Surg*. Published online May 6, 2021. doi:10.1001/jamaoto.2021.0615

2. Benmiloud F, Godiris-Petit G, Gras R, et al. Association of autofluorescence-based detection of the parathyroid glands during total thyroidectomy with postoperative hypocalcemia risk: results of the PARAFLUO multicenter randomized clinical trial. *JAMA Surg*. 2020;155(2):106-112. doi:10.1001/jamasurg.2019.4613

3. Spartalis E, Ntokos G, Georgiou K, et al. Intraoperative indocyanine green (ICG) angiography for the identification of the parathyroid glands: current evidence and future perspectives. *In Vivo*. 2020;34(1):23-32. doi:10.21873/invivo.11741

4. Zaidi N, Bucak E, Okoh A, Yazici P, Yigitbas H, Berber E. The utility of indocyanine green near infrared fluorescent imaging in the identification of parathyroid glands during surgery for primary hyperparathyroidism. *J Surg Oncol*. 2016;113(7):771-774. doi:10.1002/jso.24240

5. Kim SW, Lee HS, Lee KD. Intraoperative real-time localization of parathyroid gland with near infrared fluorescence imaging. *Gland Surg*. 2017;6(5):516-524. doi:10.21037/gs.2017.05.08

6. Vahrmeijer AL, Hutteman M, van der Vorst JR, van de Velde CJH, Frangioni JV. Image-guided cancer surgery using near-infrared fluorescence. *Nat Rev Clin Oncol*. 2013;10(9):507-518. doi:10.1038/nrclinonc.2013.123

7. Nishio N, van den Berg NS, van Keulen S, et al. Optical molecular imaging can differentiate metastatic from benign lymph nodes in head and neck cancer. *Nat Commun*. 2019;10(1):5044. doi:10.1038/s41467-019-13076-7

Complications of COVID-19 Nasopharyngeal Swab Test

During the COVID-19 pandemic, numerous swab samples have been taken for SARS-CoV-2 reverse transcriptase–polymerase chain reaction (RT-PCR) testing. Nasopharyngeal sampling is considered safe, despite adjacent vital structures (eg, orbit, skull base, rich vasculature; **Figure**). However, single case reports[1-4] and clinical observations indicate the possibility of severe complications. This case series investigated the frequency and type of SARS-CoV-2 nasopharyngeal test complications.

Methods | All patients presenting to the dedicated otorhinolaryngology emergency department (ED) of Helsinki University Hospital Department of Otorhinolaryngology–Head and Neck Surgery between March 1 and September 30, 2020, were retrospectively screened for complications after SARS-CoV-2 nasopharyngeal swab sampling. Those experiencing sampling complications underwent medical record review.

The number of SARS-CoV-2 tests performed in the catchment population (1.6 million people) of the Helsinki University Hospital during the same time period was obtained from the Finnish Institute for Health and Welfare. This study was approved by the Research Administration of Helsinki University Hospital (HUS/58/2020). As this was a retrospective registry study with no patient intervention, ethics committee approval and informed consent were not required by Finnish national legislation in accordance with the Medical Research Act of Finland 488/1999.

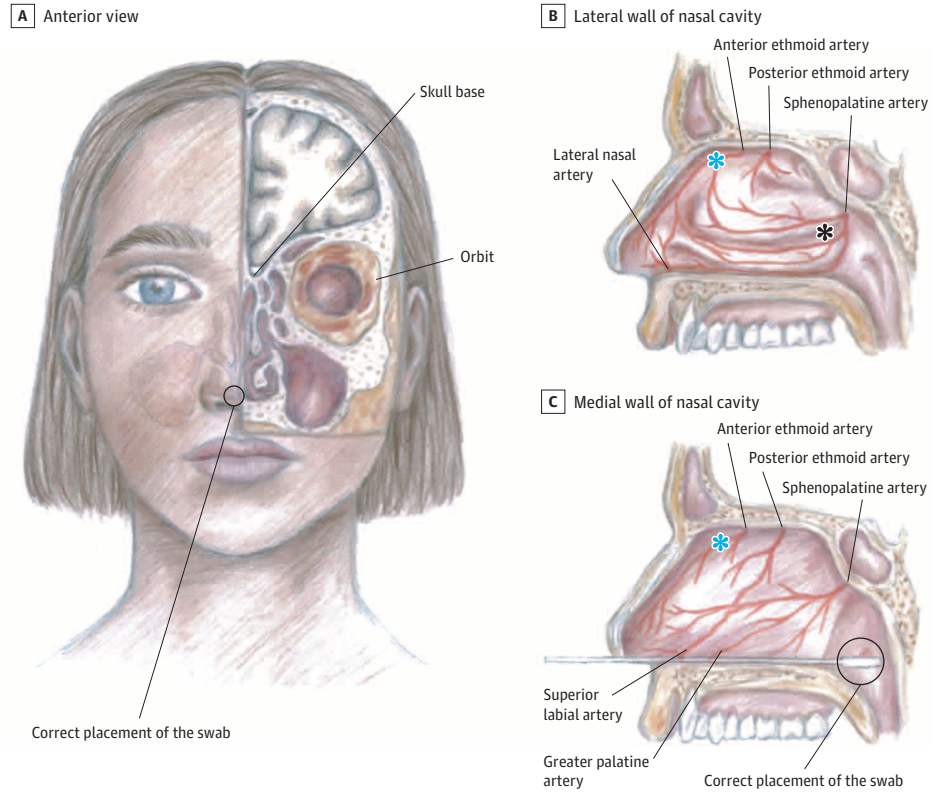
Results | During the 7-month study period, 643 284 SARS-CoV-2 RT-PCR tests were performed. Eight complication-related visits (7 females, 1 male; age range, 14.0-78.6 years; mean [SD] age, 39.5 [20.9] years) were identified in 2899 otorhinolaryngology ED patients—4 nasal bleeds and 4 broken swabs, all occurring immediately after sampling (**Table**). None of these 8 patients tested positive for COVID-19.

The frequency of complications requiring treatment in the ED was 1.24 per 100 000 performed SARS-CoV-2 tests. The broken swabs were removed via nasal endoscopy under local anesthesia, whereas the nasal bleeds required medication, numerous nasal packings, and surgical and endovascular procedures and led to fetal risk, sepsis, and blood transfusions (Table). Half of the bleeds were potentially life threatening (hemoglobin level fell below 6.5 g/dL [to convert to g/L, multiply by 10.0]). Massive bleeding complicated localization of the bleeds (shown in Figure). Infections, as well as intranasal adhesions and septal perforations, likely resulted from the repetitive nasal packings.

Discussion | Timely and reliable testing is important in controlling the COVID-19 pandemic. Nasopharyngeal swab RT-PCR testing is often used as the main diagnostic test method because it yields early results with moderate sensitivity and excellent specificity.[5]

The frequency of complications was extremely low in this study. All complications seemed to involve an incorrect sampling technique: excess use of force or an overly cranial direc-

Figure. Anatomical Structures Related to Nasopharyngeal Sampling



Correct placement of the swab and origins of the nasal bleeds in this study. The life-threatening bleeds resulted from the anterior ethmoid artery, 1 from the lateral and 1 from the medial nasal wall (blue asterisks). One bleed resulted from the sphenopalatine artery (black asterisk), and in 1 case, the bleeding site could not be identified. A, Anterior view; B, Lateral wall of nasal cavity; C, Medial wall of nasal cavity.

Table. Treatment and Sequelae of 8 Patients Treated for Complications After SARS-CoV-2 Nasopharyngeal Swab Test

Clinical event	Specific occurrence	Measure of occurrence			
Predisposing condition		Broken swab (n = 4)		Epistaxis (n = 4)	
Previous rhinosurgery	Septoplasty	1		1	
Rhinologic disorder	Nasal congestion	1		1	
	Septal deviation	1		1	
Hematologic disorder	Idiopathic thrombocytopenic purpura	0		1	
Cardiovascular disease	Coronary heart disease	1		1	
Medication	Anticoagulant	1		1	
Other	Pregnancy	0		1	
Treatment and sequelae in patients with broken swabs		**Patient**			
		1	**2**	**3**	**4**
Procedure (local anesthesia)	Removal of the broken swab	1	1	0[a]	1
Complications	NA	No	No	No	No
Diagnostic, treatment, and sequelae in patients with epistaxis		**Patient**			
		5	**6**	**7**	**8**
Blood loss	Hemoglobin level, g/dL	6.4	6.4	9.6	10.2
Procedure (local anesthesia)	Anterior nasal packing	3	3	7	0
	Posterior nasal packing	2	0	0	0
	Bipolar coagulation	1	0	3	0

(continued)

tion of the swab. While the patients who experienced broken swabs fared well, the patients with epistaxis had rockier recuperations. The complications also exposed personnel to the risk of an aerosol-generating procedure.

Table. Treatment and Sequelae of 8 Patients Treated for Complications After SARS-CoV-2 Nasopharyngeal Swab Test (continued)

Clinical event	Specific occurrence	Measure of occurrence			
Surgical (general anesthesia)	Anterior ethmoidal artery ligation	1	0	0	0
	Posterior nasal packing	0	1	0	0
	Bipolar coagulation	0	1	0	0
Endovascular procedures	Sphenopalatine artery embolization	0	0	1	0
Medication	Local hemostatic	0	3	1	1
	Systemic antibiotics	Yes	Yes	Yes	0
	Local antibiotics	0	Yes	0	0
	Iron supplements (oral or intravenous)	Yes	Yes	Yes	No
Blood transfusion	Red blood cells, 49 g Hb/unit	6	2	1	0
Complication	Local infection	Yes	Yes	Yes	No
	Systemic infection	No	No	Yes[b]	No
	Septum perforation, scarring	0	1	0	0

Abbreviations: Hb, hemoglobin; NA, not applicable.

[a] Patient swallowed the broken tip of the swab during the procedure.

[b] *Staphylococcus aureus* sepsis.

Literature regarding SARS-CoV-2 sampling complications is scarce. Breaking of the swab tip has resulted in a foreign body in the nasal cavity,[1] the esophagus[2] and, after sampling through tracheostomy, the bronchus.[3] A case of test-related cerebrospinal fluid leak, probably owing to preexisting encephalocele, has been reported.[4]

Sampling should always be performed bearing in mind the anatomical structures of the nasal cavity and its surroundings to ensure safe sampling and correct results.[5,6] Force should never be used, especially in patients with known prior operations of the nose or skull base. The sampling swab should be directed along the nasal floor, not too laterally nor too cranially, until resistance is encountered (Figure).[6]

The retrospective setting is a limitation of this study. It should be noted that Finland has a national public health service. Of the Helsinki University Hospital's catchment population (1.6 million), all severe acute otorhinolaryngology problems are treated solely in our 1 ED. Patients presenting with minor complications may have been treated at other facilities, but we did not have access to this information. Furthermore, no private otorhinolaryngologist offices have been open for patients with suspected COVID-19. Nevertheless, this study is an apt representation of patients with SARS-CoV-2 nasopharyngeal swab test complications in a large tertiary care referral center.

Based on the results, the risk for a severe complication requiring specialist-level care after SARS-CoV-2 nasopharyngeal swab testing is extremely low. Nonetheless, complications involve anatomically challenging locations and may be life threatening. To avoid complications, correct sampling techniques are crucial.

Anni Koskinen, MD, PhD
Morag Tolvi, MD, PhD
Maria Jauhiainen, MD
Eliisa Kekäläinen, MD, PhD
Anu Laulajainen-Hongisto, MD, PhD
Satu Lamminmäki, MD, PhD

Author Affiliations: Department of Otorhinolaryngology–Head and Neck Surgery, Helsinki University Hospital and University of Helsinki, Helsinki, Finland (Koskinen, Tolvi, Jauhiainen, Laulajainen-Hongisto, Lamminmäki); HUS Diagnostic Center, HUSLAB, Clinical Microbiology, Helsinki University Hospital, Helsinki, Finland (Kekäläinen).

Accepted for Publication: March 15, 2021.

Published Online: April 29, 2021. doi:10.1001/jamaoto.2021.0715

Corresponding Author: Anni Koskinen, MD, PhD, Department of Otorhinolaryngology–Head and Neck Surgery, Helsinki University Hospital, PO Box 263, FI-00029, Helsinki, Finland (anni.koskinen@hus.fi).

Author Contributions: Dr Lamminmäki had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: All authors.
Administrative, technical, or material support: All authors.
Supervision: Lamminmäki.

Conflict of Interest Disclosures: None reported.

Additional Contributions: The authors wish to thank Martta Lamminmäki for the medical illustrations. She did not receive compensation.

1. Mughal Z, Luff E, Okonkwo O, Hall CEJ. Test, test, test—a complication of testing for coronavirus disease 2019 with nasal swabs. *J Laryngol Otol*. 2020;134(7):646-649. doi:10.1017/S0022215120001425

2. De Luca L, Maltoni S. Is naso-pharyngeal swab always safe for SARS-CoV-2 testing? an unusual, accidental foreign body swallowing. *Clin J Gastroenterol*. 2021;14(1):44-47. doi:10.1007/s12328-020-01236-y

3. Hussain MH, Siddiqui S, Mahmood S, Valsamakis T. Tracheal swab from front of neck airway for SARS-CoV-2; a bronchial foreign body. *BMJ Case Rep*. 2020;13(8):e237787. doi:10.1136/bcr-2020-237787

4. Sullivan CB, Schwalje AT, Jensen M, et al. Cerebrospinal fluid leak after nasal swab testing for coronavirus disease 2019. *JAMA Otolaryngol Head Neck Surg*. 2020;146(12):1179-1181. doi:10.1001/jamaoto.2020.3579

5. Green DA, Zucker J, Westblade LF, et al. Clinical performance of SARS-CoV-2 molecular tests. *J Clin Microbiol*. 2020;58(8):e00995-20. doi:10.1128/JCM.00995-20

6. Higgins TS, Wu AW, Ting JY. SARS-CoV-2 nasopharyngeal swab testing—false-negative results from a pervasive anatomical misconception. *JAMA Otolaryngol Head Neck Surg*. 2020;146(11):993-994. doi:10.1001/jamaoto.2020.2946

Preliminary Analysis of Association Between COVID-19 Vaccination and Sudden Hearing Loss Using US Centers for Disease Control and Prevention Vaccine Adverse Events Reporting System Data

Many vaccine-related adverse events are associated with otolaryngologic manifestations. In particular, the incidence of sudden sensorineural hearing loss (SSNHL) was examined after influenza vaccination in a large-scale study that demonstrated