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Structured training program on confocal laser endomicroscopy for pancreatic cystic lesions: a multicenter prospective study among early-career endosonographers (with video)

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Abstract

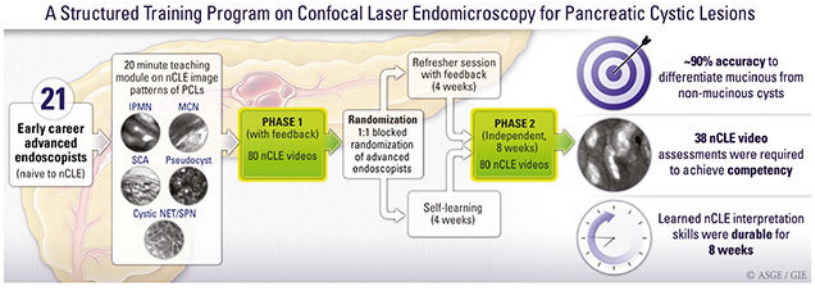
Background and Aims: Data on how to teach endosonographers needle-based confocal laser endomicroscopy (nCLE)-guided histologic diagnosis of pancreatic cystic lesions (PCLs) are limited. Hence, we developed and tested a structured educational program to train early-career endosonographers in nCLE-guided diagnosis of PCLs.

Methods: Twenty-one early-career nCLE-naive endosonographers watched a teaching module outlining nCLE criteria for diagnosing PCLs. Participants then reviewed 80 high-yield nCLE videos, recorded diagnoses, and received expert feedback (phase 1). Observers were then randomized to a refresher feedback session or self-learning at 4 weeks. Eight weeks after training, participants independently assessed the same 80 nCLE videos without feedback and provided histologic predictions (phase 2). Diagnostic performance of nCLE to differentiate mucinous versus nonmucinous PCLs and to diagnose specific subtypes were analyzed using histopathology as the criterion standard. Learning curves were determined using cumulative sum analysis.

Results: Accuracy and diagnostic confidence for differentiating mucinous versus nonmucinous PCLs improved as endosonographers progressed through nCLE videos in phase 1 ($P < .001$). Similar trends were observed with the diagnosis of PCL subtypes. Most participants achieved competency interpreting nCLE, requiring a median of 38 assessments (range, 9-67). During phase 2, participants independently differentiated PCLs with high accuracy (89%), high confidence (83%), and substantial interobserver agreement ($\kappa = .63$). Accuracy for nCLE-guided PCL subtype diagnoses ranged from 82% to 96%. The learned nCLE skills did not deteriorate at 8 weeks and were not impacted by a refresher session.

Conclusions: We developed a practical, effective, and durable educational intervention to train early-career endosonographers in nCLE-guided diagnosis of PCLs.

Graphical Abstract



Pancreatic cystic lesions (PCLs) are highly prevalent and are a common reason for referral to gastroenterologists.[1,2] Each PCL subtype carries a different biologic behavior that ranges from benign (serous cystadenoma [SCA], pseudocyst) and premalignant (intraductal papillary mucinous neoplasms [IPMNs], mucinous cystic neoplasms [MCNs]) to neoplastic (cystic neuroendocrine tumor [cystic NET], solid pseudopapillary tumor [SPN]). Unfortunately, histologic diagnosis is rarely available to guide treatment decisions, and clinicians ultimately rely on diagnostic tests (cross-sectional images, EUS, fluid analysis) that are suboptimal in determining the specific type of PCL.[3] Inaccurate diagnoses can result in unnecessary surgeries, missed malignancy, high healthcare costs, and psychological distress.[4–7]

EUS-guided needle-based confocal laser endomicroscopy (nCLE) is an endoscopic technology that provides in vivo histologic assessment of the inner epithelium, enabling virtual histologic diagnosis of PCLs.[8–10] In expert hands, EUS-nCLE has been shown to be safe and highly accurate in differentiating mucinous from nonmucinous cysts and in diagnosing common PCL subtypes.[9–13] A recent network meta-analysis that included 40 studies and over 3500 patients revealed that EUS-nCLE has the highest accuracy in diagnosing PCLs compared with other tests.[14] Accurate nCLE-guided diagnosis reduces unwarranted resection of benign PCLs and is associated with cost savings as shown in a recent study.[15]

One of the barriers for wider adoption of EUS-nCLE in clinical practice is the lack of structured training during advanced endoscopy fellowship and post-training clinical practice. To achieve high diagnostic accuracy, effective educational tools are needed for endosonographers to achieve competency in the real-time nCLE-guided characterization of PCLs. A recent study demonstrated that teaching nCLE patterns to nonendosonographers was feasible with a teaching module and active feedback, resulting in high diagnostic accuracy in differentiating mucinous from nonmucinous PCLs.[16] However, the study did not involve endosonographers and did not evaluate proficiency in EUS-guided diagnosis of PCL subtypes. Moreover, the learning curve among endosonographers in the histologic classification of PCLs with nCLE has yet to be studied. It is also unknown whether a training module results in durable interpretation skills and whether a refresher feedback session can enhance the durability of the initial training.

In this study, we hypothesized that an audiovisual teaching module in combination with nCLE video clip assessments and targeted feedback would result in significant improvement in the performance of endosonographers in nCLE-guided virtual histologic diagnosis of PCLs. Our specific aims were to assess the impact of an audiovisual teaching module on the performance of early-career endosonographers in differentiating mucinous from nonmucinous PCLs and diagnosing PCL subtypes with nCLE, to define the learning curve of endosonographers to achieve competency in nCLE-guided PCL differentiation of mucinous from nonmucinous PCLs, to demonstrate the durability of nCLE training over an 8-week period, and to evaluate the impact of a refresher feedback session on durability.

METHODS

Study design

This was a multicenter, prospective, educational study conducted among early-career endosonographers in 2021. EUS-nCLE subject videos for training and assessments were obtained from 3 prospective studies: CONTACT, a French multicenter study of 206 patients conducted from 2012 to 2016 (clinicaltrials.gov NCT01563133); INDEX, a U.S. single-center study of 144 patients from 2015 to 2018 (clinicaltrials.gov NCT02516488); and CLIMB, a U.S. multicenter study started in 2018 and continuing to the present (clinicaltrials.gov NCT03492151). The institutional review board of each participating center from these 3 cohorts approved the study protocol.

Participants

Advanced endoscopy fellows and advanced endoscopists within 3 years of starting independent practice were eligible to participate. We excluded endosonographers with nCLE experience or prior formal training in nCLE-guided evaluation of PCLs. To maintain homogeneity in the study population and given the uniform structure of advanced endoscopy training in the United States, endosonographers receiving advanced endoscopy training or practicing outside the United States were ineligible. A list of potential participants was created by the study investigators (J.D.M. and S.G.K.). Enrollment was conducted by e-mail invitations to potential participants and through social media postings.

Teaching module

An online 20-minute audiovisual teaching module was prepared by an endosonographer with extensive experience in nCLE assessments of PCLs (S.G.K.) and uploaded to youtube.com (Google, Mountain View, Calif, USA) (Video 1, available online at www.giejournal.org). This instructional video outlined previously validated nCLE imaging criteria to diagnose the most common PCL subtypes:

1. Finger-like papillary structures in IPMNs[9,17–21]
2. Layered epithelial bands in MCNs[9,18,20,21]
3. Trabecular pattern with nests of cells in cystic NETs and SPNs[9,10,13]
4. Superficial vascular pattern or fern-like pattern of vascularity in SCAs[9,10,13,19,22,23]

5. Bright particles against a dark background and clumps of inflammatory cells in pseudocysts[18]

The presentation included several case studies of nCLE in PCLs, explained atypical nCLE patterns, and covered reasons for pattern misinterpretation. The nCLE images used in this instructional video were different from the cases used for assessments.

nCLE videos

All EUS-nCLE procedures were performed by endosonographers with significant experience in nCLE for PCLs (>25 cases) and using local standardized protocols.[13] For the present study, we selected 80 videos of subjects who had definitive histopathologic diagnosis of the most prevalent PCLs with representative nCLE patterns. Each nCLE video was shortened to a high-yield clip of <1 minute that best represented the PCL epithelium using a previously described methodology.[10,19]

Educational intervention

Phase 1.—The study flow chart is shown in Figure 1. All participants first viewed the audiovisual teaching module and subsequently watched and assessed each of the 80 randomly arranged nCLE videos without clinical information using Qualtrics (Qualtrics XM, Provo, Utah, USA). Participants indicated whether the cyst was mucinous or nonmucinous. If the cyst was considered mucinous, participants needed to specify whether it was an IPMN or MCN. If participants diagnosed the cyst as nonmucinous, they needed to determine the subtype (pseudocyst, SCA, or cystic NET/SPN). Cystic NETs and SPNs were grouped into 1 category because of their similar nCLE appearances. Subsequently, participants rated their diagnostic confidence in each assessment as either high or low. After participants completed each set of 10 videos, the senior investigator (S.G.K.) provided interactive feedback about cyst histology and reviewed supportive nCLE patterns of each video. This interactive feedback session was conducted live using Zoom (Zoom Video Communications, San Jose, Calif, USA).

Randomization.—After phase 1, participants were randomized in a 1:1 ratio, stratified by level of training (advanced endoscopy fellows or practicing advanced endoscopists), and using blocks of 4 participants to a refresher feedback session or self-learning. Participants in the refresher feedback group reviewed 20 nCLE videos at 4 weeks from phase 1 and received prerecorded targeted expert feedback. Those randomized to self-learning were provided 20 nCLE videos at 4 weeks for self-review but did not receive feedback. These 20 nonstudy nCLE videos were different from the cases used for assessments.

Phase 2.—Eight weeks after phase 1, participants viewed the 80 study nCLE videos rearranged randomly to avoid recollection bias and recorded their prediction of PCL histology and degree of diagnostic confidence using Qualtrics. No feedback session was provided in this phase to assess the durability of training provided in phase 1.

Statistical analysis

To detect an improvement in diagnostic accuracy from 70% to 80% between phases 1 and 2, with a Type I error of .05 and power of 90%, a minimum of 411 observations were needed at each phase or at least 6 participants assessing the 80 videos. The diagnostic performance of nCLE was evaluated by comparing histologic predictions with confirmatory histopathology as the criterion standard. Sensitivity, specificity, and accuracy of nCLE to differentiate mucinous from nonmucinous PCLs and to diagnose cyst subtypes were calculated. Interobserver agreement (IOA) was estimated using Fleiss' kappa, and kappa values were interpreted according to the Landis and Koch scale: <0, no agreement; 0 to .20, slight agreement; .21 to .40, fair agreement; .41 to .60, moderate agreement; .61 to .80, substantial agreement; and .81 to 1, almost perfect agreement.[24] To evaluate the impact of training, the Cochran-Armitage test for trend was used to determine if diagnostic performance and degree of diagnostic confidence improved as trainees progressed through blocks of 20 videos (1-20 vs 21-40 vs 41-60 vs 61-80) in each phase. To assess the durability of initial training, the χ^2 test was used to compare results between both study phases. To test the effect of the refresher feedback intervention, the χ^2 test was used to compare phase 2 results between those randomized to a refresher session or to self-learning.

A cumulative sum (CUSUM) analysis was applied to assess the learning curve for each endosonographer to differentiate mucinous from nonmucinous PCLs using nCLE. An acceptable and unacceptable level of incorrect responses was set at 10% and 30%, respectively, by assigning an acceptable failure rate of $p_0 = .10$, an unacceptable failure rate of $p_1 = .30$, Type I and II errors = .10, and then s = .19 and 1-s = .81. The cumulative failure was plotted against the 80 consecutive videos with acceptable and unacceptable lines drawn within the CUSUM plot. Competency was achieved if the CUSUM plot fell below the acceptable line. Performance was unacceptable if the CUSUM plot rose above the unacceptable line and inconclusive with further training recommended if the plot stayed between the 2 boundary lines. Statistical analyses were performed using R version 4.1.2 (*R* Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline characteristics

Twenty-one early-career endosonographers were included: 10 advanced endoscopy fellows in training and 11 practicing advanced endoscopists (Fig. 1). Most participants (86%) were from academic centers. After phase 1, 11 participants were randomized to a refresher feedback session and 10 to self-learning, with a similar distribution of advanced endoscopy fellows in both groups (5 per group). The assessments in both study phases were conducted using representative nCLE videos of 53 patients with mucinous PCLs (IPMN = 37, MCN = 16) and 27 with nonmucinous PCLs (SCA = 11, pseudocyst = 3, cystic NET/SPN = 13) with confirmed histopathology.

Phase 1: nCLE video assessments with targeted feedback

The diagnostic performance and confidence of participants for nCLE-guided differentiation of mucinous from nonmucinous PCLs and prediction of cyst subtypes are shown in Table

1. A significant improvement in sensitivity ($P < .001$), specificity ($P = .005$), accuracy ($P < .001$), and high diagnostic confidence ($P < .001$) to differentiate mucinous from nonmucinous cysts was found as participants progressed through blocks of 20 nCLE videos. Compared with the first 20 video assessments, participants in the last 20 videos demonstrated significant improvement in accuracy (86% vs 74%, $P < .001$) and high diagnostic confidence (83% vs 63%, $P < .001$) for nCLE-guided differentiation of mucinous from nonmucinous PCLs. Accuracy was superior in high-confidence assessments compared with low-confidence predictions (91% vs 67%, $P < .001$). In the CUSUM analysis (Fig. 2A), most participants (76.2%) achieved competency in nCLE-guided differentiation of mucinous versus nonmucinous PCLs. Among these, the median number to reach competency was 38 nCLE video assessments (range, 9-67).

Similarly, the diagnostic accuracy and high diagnostic confidence to predict IPMNs, MCNs, cystic NET/SPNs, and SCAs significantly improved ($P < .05$) as participants progressed through blocks of 20 videos. For pseudocysts, the high diagnostic confidence decreased through video blocks ($P = .02$); however, diagnostic accuracy did not change ($P = .17$) and was high through all video blocks (>90%).

Phase 2: independent nCLE video assessments without feedback at 8 weeks

As participants progressed through blocks of 20 nCLE videos during phase 2 (Table 2), significant improvement was not found in diagnostic parameters to differentiate mucinous from nonmucinous PCLs and to predict cyst subtypes, suggesting a plateau in learning. During these independent assessments, participants differentiated mucinous from nonmucinous PCLs using nCLE with 89% accuracy, 91% sensitivity, and 84% specificity. The assessments to distinguish mucinous versus nonmucinous PCLs were made with substantial interobserver agreement ($\kappa = .63$) and high diagnostic confidence (83%). Compared with low-confidence assessments, the diagnostic accuracy was superior in high-confidence predictions (92% vs 70%, $P < .001$). Diagnostic accuracy was also higher in subjects who had achieved competency during phase 1 than those who had not (92% vs 79%, $P < .001$). Among those who achieved competency in phase 1, accuracy was better when diagnostic confidence was high as compared with low (94% vs 78%, $P < .001$). In the CUSUM analysis during phase 2 (Fig. 2B), 85% of participants demonstrated competency to differentiate mucinous from nonmucinous PCLs.

The overall accuracy of nCLE to diagnose specific cyst types during phase 2 was highest for pseudocysts (96%), SCAs (93%), and cystic NET/SPNs (90%) and was slightly lower for IPMNs (84%) and MCNs (82%). The IOA was moderate for IPMNs ($\kappa = .55$), pseudocysts ($\kappa = .57$), SCAs ($\kappa = .44$), and cystic NET/SPNs ($\kappa = .44$) and fair for MCNs ($\kappa = .32$).

Impact of refresher feedback session at 4 weeks

Adding a refresher feedback session at 4 weeks did not improve the diagnostic performance of nCLE at 8 weeks (Table 3). Participants in the self-learning arm demonstrated higher accuracy and substantial IOA in PCL differentiation.

Comparison of phase 1 and phase 2

During independent assessments of nCLE videos in phase 2 (Table 4), participants differentiated mucinous from nonmucinous PCLs with higher diagnostic accuracy ($P = .002$) and higher degree of confidence ($P < .001$) than in phase 1. The diagnosis of IPMN and cystic NET/SPN was made with higher confidence in phase 2 as compared with phase 1 ($P = .003$). Otherwise, there was no significant difference in accuracy, confidence, or IOA between study phases, suggesting the diagnostic nCLE interpretation skills remained durable after 8 weeks of initial training.

DISCUSSION

In this multicenter, prospective, educational study, we demonstrated that an audiovisual nCLE teaching module in combination with nCLE video assessments augmented by targeted feedback resulted in highly accurate virtual histologic diagnoses of PCLs among nCLE-naive early-career endosonographers. The application of learning curves revealed that most endosonographers reached competency at a median of 38 nCLE video assessments to accurately differentiate mucinous from nonmucinous PCLs. Finally, training in nCLE image analysis was durable for at least 8 weeks, and the absence of a refresher feedback module did not improve the durability of nCLE-guided PCL diagnosis.

In the management of PCLs, it has been demonstrated that EUS-nCLE performed by expert operators is highly accurate and cost beneficial.[9,10,12,13,15] However, data are limited in teaching nCLE, and no studies have assessed learning curves or competency of this imaging biomarker among endosonographers. In a recent single-center study, our group demonstrated among 18 nonendosonographers that a teaching module of nCLE-guided diagnosis and 20 training assessments with feedback resulted in high diagnostic accuracy for differentiating mucinous from nonmucinous PCLs.[16] The present study confirms in a large cohort of early-career endosonographers from multiple centers that nCLE-guided diagnosis of PCLs can be learned with a focused teaching module and active feedback. This is clinically relevant because the lack of structured training has been 1 reason for the limited use of EUS-nCLE in practice. Using virtual platforms, we demonstrated that remote nCLE training is simple, feasible, and effective. This can overcome some challenges with nCLE training, such as equipment not being widely available, limited local expertise, and nCLE images not being intuitive for self-learning. Similar web-based educational approaches have been used in other areas of endoscopy and surgery, especially in response to the coronavirus disease 2019 pandemic.[25,26]

An innovative aspect of this study was that we report learning curves with the required number of video assessments toachieve competency for nCLE-guided differentiation of PCLs. Using 10% as an acceptable error rate and 30% as an unacceptable error rate, we showed that most early-career endosonographers achieved competency and that 38 nCLE subject-video assessments with targeted feedback were needed to become competent. However, 23.8% of participants did not achieve competency in phase 1 and would have benefited from retraining before proceeding to independent nCLE assessments. We chose these error rate cutoffs based on data from meta-analyses reporting accuracies for EUS-

nCLE of ~ 90% and cyst fluid carcinoembryonic antigen of ~ 70% for diagnosing mucinous PCLs.[27,28]

During independent video assessments at 8 weeks, endosonographers newly trained in nCLE had 89% accuracy for differentiating PCLs, similar to estimates from recent meta-analyses.[27,29] Achieving competency during phase 1 and making high-confidence assessments were associated with higher diagnostic accuracy during independent nCLE assessments. Diagnostic accuracy was highest when those who had achieved competency in phase 1 were highly confident in their predictions (accuracy, 94%), which approximated to the high diagnostic accuracy estimates reported by expert nCLE observers (~95%).[9,12,13] Another factor that could have impacted the overall diagnostic accuracy in our study may have been increasing fatigue in participants from assessing a large number of nCLE videos (n = 80) over a short period, which is depicted by a decline in diagnostic performance during assessments of the last video block in both phases (Tables 1 and 2). Although the accuracy of nCLE to differentiate mucinous from nonmucinous PCLs among newly trained endosonographers was higher than cyst fluid carcinoembryonic antigen (~70%), it was not superior to cyst fluid glucose (94%) or molecular analysis (97%).[30,31] However, nCLE offers higher specificity than cyst glucose (84% vs 65%) and better sensitivity than molecular analysis (91% vs 79%), for which nCLE has been considered the optimal modality to diagnose mucinous PCLs in recent network meta-analyses.[14,32]

The ability to diagnose PCL subtypes is an advantage of EUS-nCLE over conventional diagnostic approaches (cross-sectional images, EUS, cyst fluid cytology, concentration of glucose, or carcinoembryonic antigen). In this study, we demonstrated that our educational intervention allowed endosonographers to learn validated nCLE imaging criteria for diagnosing prevalent PCL subtypes. During independent assessments, the diagnostic accuracies of early-career endosonographers participating in this study were comparable with experts from a recent international study using a similar video library (experts vs trainees: SCA, 98% vs 93%; cystic NET/SPN, 96% vs 90%; pseudocyst, 96% vs 96%; IPMN, 86% vs 84%; MCN, 84% vs 82%).[12] The high accuracy of nCLE in diagnosing SCAs, NET/SPNs, and pseudocysts was primarily driven by its high specificity (93%-97%). This means that nCLE is valuable in “ruling in” these PCL subtypes with a low rate of false-positive interpretations. However, this high specificity comes at the expense of low sensitivity (65%-73%), which was lower than the previous estimates reported by nCLE experts (88%-97%).[12] The sensitivity of nCLE to diagnose SCAs demonstrated improvement over the training session, although a decline was observed during the last video block of assessments. This decline could potentially be attributed to variations in imaging patterns within a small subset of cases, increasing observer fatigue, or the novelty of the imaging technique itself for inexperienced observers. The use of molecular analysis, either alone or in conjunction with nCLE, can provide valuable insights into the diagnosis of PCL subtypes by detecting specific genomic alterations associated with mucinous cysts, SCAs, and cystic NETs.[33] However, it is important to note that the availability of this approach is currently limited. The use of EUS through-the-needle biopsy sampling can also provide histologic diagnosis of PCLs; however, its use has been associated with a higher risk of adverse events than nCLE (~ 10% vs ~ 3%) and should be used with caution.[14,34]

A concern with any educational intervention is that the skills learned by participants may gradually diminish over time. This is particularly relevant when the skillset is infrequently used in endoscopic practice. To assess this issue, we compared the performance of endosonographers between both study phases and found sustained durability of nCLE skills for 8 weeks. This is important for credentialing and competency, because exposure to EUS-nCLE cases at least every 8 weeks may mitigate the dilution of skillsets necessary for nCLE-guided diagnosis of PCLs. It is possible that interruptions and lack of nCLE exposure longer than 8 weeks may result in decrements in competency. However, this was not evaluated in our study and deserves future research. We also evaluated if the introduction of a refresher feedback session at 4 weeks could prevent the decrement of nCLE skills at 8 weeks and found this to be ineffective.

This structured training intervention of a novel imaging biomarker for diagnosing PCLs has several limitations. Primarily, this method lacks training in the technical aspects of performing a high-quality EUS-nCLE examination. However, attaining competency in nCLE image interpretation is a critical requisite before performing EUS-nCLE because it will conceptually improve procedural aspects, including image acquisition. The teaching module and targeted feedback were provided by a single expert in nCLE, which may impact the reproducibility of this intervention. However, designing an online teaching module with prerecorded feedback may be possible to make our intervention reproducible and widely available, as this has been shown to be noninferior to real-time feedback.[16] Training and competency assessments were conducted using edited high-yield nCLE videos obtained by experts to remove variability in technique and to purely assess performance on image interpretation. This may have resulted in higher accuracy rates than expected in clinical practice. Therefore, our results may not be generalizable to real-time EUS-nCLE procedures performed by novice operators. Observer selection bias could have been introduced by including only early-career endosonographers from the United States or by recruiting subjects through e-mail and social media. Patient selection bias is inherent by using nCLE videos of common PCLs with validated nCLE patterns and confirmed histopathology. However, study methodology for observer and patient selection reduced confounding and misclassification bias, respectively. Notwithstanding, unmeasured confounders such as prior exposure or knowledge of nCLE and variable motivation to learn nCLE are possible and may partly explain the inefficacy of the refresher feedback intervention. Although we did not formally assess learning curves for each PCL subtype, our results suggest that the teaching module and 80 subject-video assessments with targeted feedback were sufficient to train endosonographers in nCLE-guided diagnosis of specific PCL subtypes. Although recent studies have demonstrated that nCLE can differentiate the degree of dysplasia in IPMNs,[19,35] this study did not evaluate training endosonographers in this aspect. We are currently in the process of testing a structured educational tool for the differentiation of dysplasia in IPMNs.

Despite these limitations, our study has several strengths. To the best of our knowledge, this is the first structured training for educating endosonographers in nCLE-guided diagnosis of PCLs, assessing learning curves for competency, and evaluating durability of the learned imaging interpretation skills. We included a considerable number of early-career endosonographers with variable levels of EUS experience and from different institutions,

which increases the external validity of our findings. We used a large cohort of different cyst types with definitive histopathologic diagnosis as the criterion standard to decrease the risk of misclassification bias. Finally, we applied randomization methods to reduce bias in assessing the role of a refreshing training session in durability of learning.

We conclude that using a remote educational intervention that combines a teaching module, a video library of high-yield nCLE videos, and targeted expert feedback can effectively teach early-career endosonographers to accurately diagnose the most prevalent PCLs with EUS-nCLE. In addition, the educational intervention resulted in durable nCLE image interpretation skills that can last for at least 8 weeks. The strategy applied in this study can serve as a prelude in training endosonographers before performing EUS-nCLE in clinical practice, because accurate interpretation can lead to high-quality image acquisition. Future studies need to assess interventions to train endosonographers in the procedural aspects of EUS-nCLE, to evaluate learning curves for real-time nCLE assessments, and to examine the impact of artificial intelligence in nCLE-guided diagnosis of pancreatic cysts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations:

CUSUM	cumulative sum
IOA	interobserver agreement
IPMN	intraductal papillary mucinous neoplasm
MCN	mucinous cystic neoplasm
nCLE	needle-based confocal laser endomicroscopy
NET	neuroendocrine tumor
PCL	pancreatic cystic lesion
SCA	serous cystadenoma
SPN	solid pseudopapillary tumor

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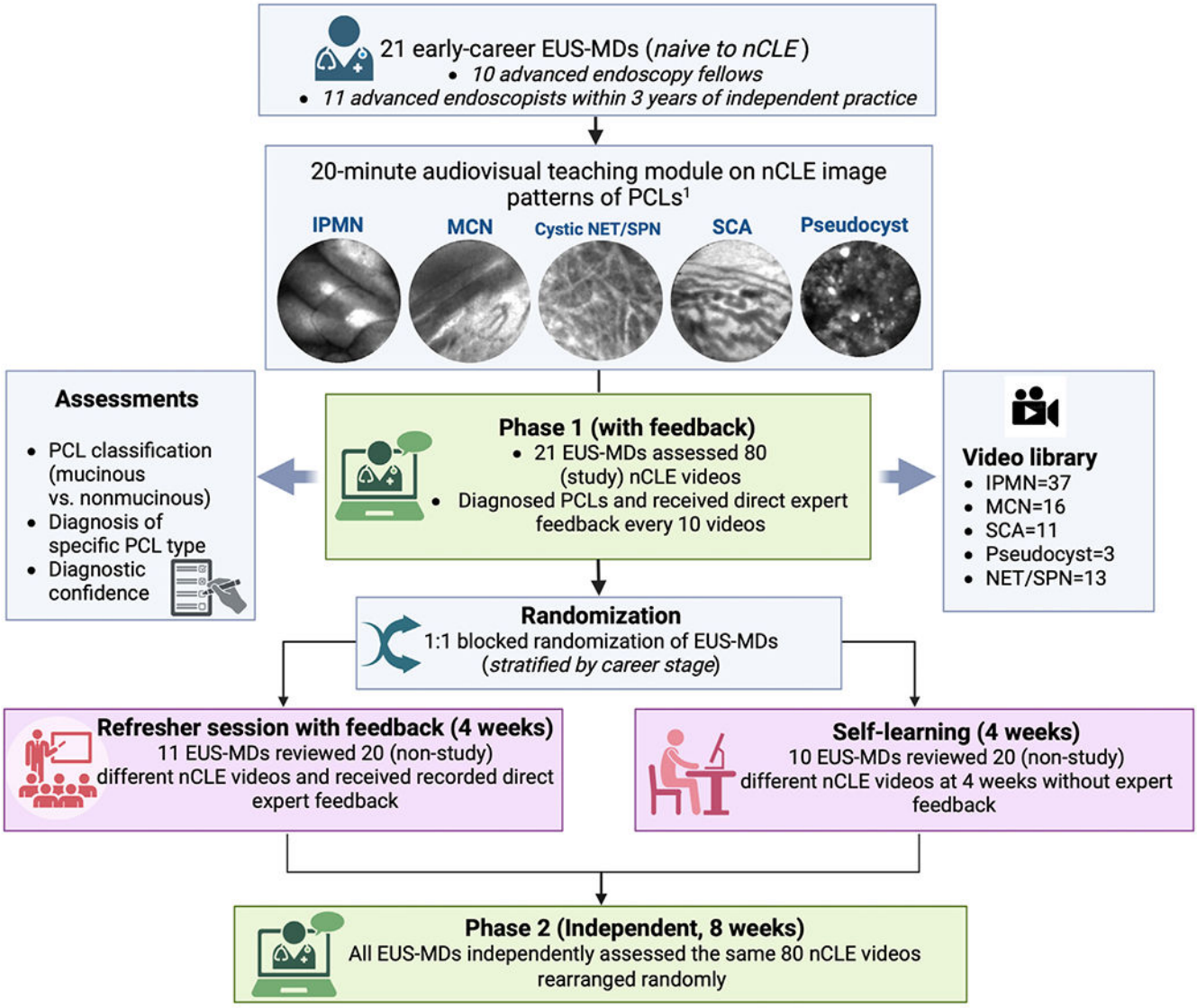

Figure 1.

Study flowchart. *EUS-MDs*, Endosonographers; *PCL*, pancreatic cystic lesion; *nCLE*, needle-based confocal laser endomicroscopy; *IPMN*, intraductal papillary mucinous neoplasm; *MCN*, mucinous cystic neoplasms; *SCA*, serous cystadenoma; *NET*, cystic neuroendocrine tumor; *SPN*, solid pseudopapillary neoplasm.

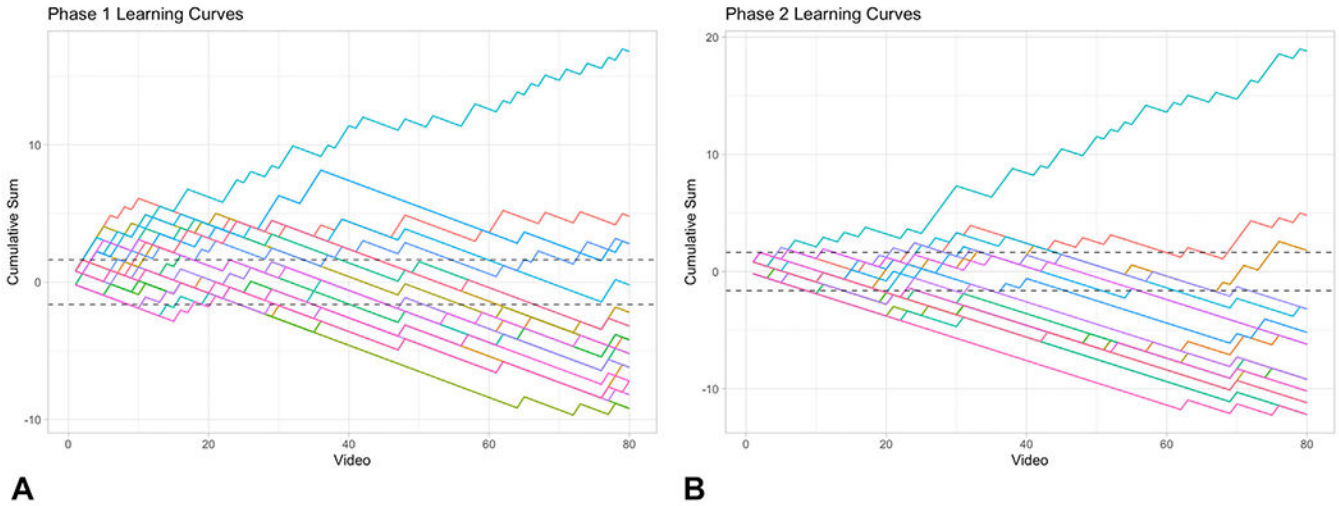

Figure 2.

Cumulative sum analysis of (**A**) phase 1 and (**B**) phase 2 learning curves among early-career endosonographers for differentiating mucinous versus nonmucinous pancreatic cystic lesions with EUS-guided needle-based confocal laser endomicroscopy. Each individual *colored line* represents 1 endosonographer. Crossing the *lower dashed line* indicates performance within the acceptable rate of 10% (achieved competency), crossing the *upper dashed line* suggests an unacceptable rate of 30% (requires retraining), and results between these 2 thresholds indicate the need for ongoing observation.

TABLE 1.

Diagnostic performance and high confidence predictions for needle-based confocal laser endomicroscopy–guided diagnosis of pancreatic cystic lesions by video block during phase 1 (assessments with feedback)

		Phase 1 video block				
	Overall	**1-20**	**21-40**	**41-60**	**61-80**	***P* value***
Mucinous vs nonmucinous						
Sensitivity	86 (84-88)	74 (69-80)	86 (83-90)	92 (89-95)	90 (87-94)	<.0001
Specificity	82 (79-85)	72 (66-79)	85 (78-92)	97 (94-100)	79 (72-86)	.0054
Accuracy	85 (83-87)	74 (69-78)	86 (83-89)	94 (91-96)	86 (83-90)	<.0001
High confidence	76 (74-78)	63 (58-67)	73 (68-77)	85 (81-88)	83 (79-86)	<.0001
Intraductal papillary mucinous neoplasm						
Sensitivity	78 (75-81)	53 (47-60)	80 (74-85)	97 (94-100)	89 (85-94)	<.0001
Specificity	88 (86-90)	90 (85-94)	86 (81-91)	86 (81-90)	91 (88-95)	.2875
Accuracy	84 (82-85)	71 (67-76)	83 (79-86)	90 (87-93)	90 (88-93)	<.0001
High confidence	66 (64-68)	51 (47-56)	61 (57-66)	71 (67-76)	76 (72-80)	<.0001
Mucinous cystic neoplasms						
Sensitivity	57 (52-62)	71 (52-91)	40 (30-51)	56 (47-64)	69 (60-77)	.0073
Specificity	88 (86-90)	81 (77-85)	87 (83-91)	98 (96-100)	89 (86-93)	<.0001
Accuracy	82 (80-84)	81 (77-84)	78 (74-82)	85 (82-89)	84 (81-88)	.018
High confidence	41 (39-44)	36 (31-40)	41 (36-46)	34 (30-39)	52 (47-57)	.0207
Cystic neuroendocrine tumor or solid pseudopapillary neoplasm						
Sensitivity	60 (55-66)	27 (16-38)	67 (57-77)	81 (71-91)	65 (53-77)	<.0001
Specificity	93 (91-94)	89 (85-92)	90 (87-93)	98 (97-99)	94 (92-97)	<.0001

	Overall	Phase 1 video block				*P* value*
		1-20	21-40	41-60	61-80	
Accuracy	88 (86-89)	79 (75-83)	85 (82-89)	95 (93-97)	90 (87-93)	<.0001
High confidence	41 (39-43)	33 (28-37)	33 (28-37)	50 (45-55)	52 (48-57)	.0026
Pseudocyst						
Sensitivity	76 (66-87)	95 (89-102)	38 (17-59)	†	†	<.0001
Specificity	96 (95-97)	96 (94-98)	95 (93-97)	95 (93-97)	96 (95-98)	.3632
Accuracy	95 (94-96)	96 (94-98)	92 (90-95)	95 (93-97)	96 (95-98)	.1721
High confidence	53 (50-55)	71 (67-75)	39 (35-44)	20 (16-24)	53 (49-58)	.0024
Serous cystadenoma						
Sensitivity	70 (64-76)	55 (44-65)	†	94 (88-100)	68 (58-78)	.0041
Specificity	95 (94-96)	89 (86-92)	96 (95-98)	98 (96-99)	97 (96-99)	<.0001
Accuracy	92 (90-93)	82 (78-86)	96 (95-98)	97 (96-99)	91 (89-94)	<.0001
High confidence	54 (51-56)	40 (35-44)	33 (29-38)	69 (64-73)	61 (56-65)	.0005

Values are % (95% confidence interval).

**P* value from 1-sided Cochran-Armitage test.

†Value does not exist because there were no true positives and no false negatives within the video block for the cyst subtype.

TABLE 2.

Diagnostic performance and high confidence predictions for needle-based confocal laser endomicroscopy–guided diagnosis of pancreatic cystic lesions by video block during phase 2 (independent assessments)

		Phase 2 video block				
	Overall	**1-20**	**21-40**	**41-60**	**61-80**	***P* value***
Mucinous vs nonmucinous						
Sensitivity	91 (89-92)	93 (90-96)	85 (81-89)	95 (92-97)	90 (87-94)	.3249
Specificity	84 (81-88)	79 (72-85)	84 (78-91)	93 (88-97)	84 (78-89)	.0552
Accuracy	89 (87-90)	88 (85-91)	85 (81-88)	94 (92-96)	88 (85-91)	.0968
High confidence	83 (81-84)	86 (82-89)	80 (76-83)	86 (82-89)	79 (75-83)	.0592
Intraductal papillary mucinous neoplasm						
Sensitivity	80 (78-83)	82 (77-87)	83 (77-89)	80 (74-85)	75 (67-83)	.0538
Specificity	87 (84-89)	92 (88-96)	82 (77-87)	94 (90-97)	83 (78-87)	.079
Accuracy	84 (82-85)	86 (83-89)	82 (79-86)	86 (83-89)	81 (77-84)	.0614
High confidence	73 (71-75)	71 (67-76)	74 (70-78)	76 (72-80)	71 (67-75)	.4178
Mucinous cystic neoplasms						
Sensitivity	57 (52-63)	45 (23-67)	50 (41-59)	78 (68-89)	56 (47-65)	.0882
Specificity	88 (86-90)	86 (83-90)	93 (90-96)	88 (84-91)	86 (82-90)	.3894
Accuracy	82 (80-84)	84 (81-88)	80 (76-84)	87 (83-90)	77 (73-81)	.0457
High confidence	44 (41-46)	46 (41-51)	31 (27-36)	45 (41-50)	50 (46-55)	.0735
Cystic neuroendocrine tumor or solid pseudopapillary neoplasm						
Sensitivity	73 (68-78)	70 (56-84)	71 (61-81)	67 (55-79)	81 (73-90)	.085
Specificity	93 (91-94)	94 (92-97)	89 (86-93)	94 (92-97)	93 (90-96)	.4099

		Phase 2 video block				
	Overall	**1-20**	**21-40**	**41-60**	**61-80**	***P* value***
Accuracy	90 (88-91)	92 (89-94)	86 (82-89)	90 (87-93)	91 (88-94)	.4129
High confidence	57 (55-59)	49 (44-54)	64 (59-68)	56 (51-61)	55 (50-60)	.4942
Pseudocyst						
Sensitivity	73 (62-85)	85 (69-101)	†	68 (53-82)	†	.0742
Specificity	97 (96-98)	98 (96-99)	96 (94-98)	99 (98-100)	96 (93-98)	.1178
Accuracy	96 (95-97)	97 (96-99)	96 (94-98)	96 (94-98)	96 (93-98)	.0977
High confidence	52 (50-55)	64 (59-69)	40 (35-45)	60 (55-65)	33 (29-38)	.076
Serous cystadenoma						
Sensitivity	65 (58-71)	64 (53-74)	70 (56-84)	85 (69-101)	58 (47-68)	.2398
Specificity	97 (96-98)	99 (98-100)	98 (96-99)	95 (92-97)	98 (97-100)	.1093
Accuracy	93 (91-94)	92 (89-94)	95 (93-97)	94 (92-97)	90 (87-93)	.1616
High confidence	57 (55-60)	56 (52-61)	51 (46-56)	54 (49-59)	65 (61-70)	.1703

Values are % (95% confidence interval).

** P* value from 1-sided Cochran-Armitage test.

† Value does not exist because there were no true positives and no false negatives within the video block for the specified cyst type.

TABLE 3.

Diagnostic performance, confidence, and IOA of early-career endosonographers for needle-based confocal laser endomicroscopy–guided diagnosis of pancreatic cystic lesions during phase 2 by randomized assignment to refresher vs self-learning (no refresher) session

	Overall	Refresher course	Self-learning	*P* value*
Mucinous vs nonmucinous				
Sensitivity	91 (89-92)	87 (84-90)	94 (92-96)	<.0001
Specificity	84 (81-88)	80 (75-85)	89 (85-93)	.0044
Accuracy	89 (87-90)	85 (82-87)	92 (91-94)	<.0001
High confidence	83 (81-84)	80 (77-82)	86 (83-88)	.002
IOA, κ	.63 (.55-.70)	.52 (.43-.60)	.75 (.66-.83)	†
Intraductal papillary mucinous neoplasm				
Sensitivity	80 (78-83)	79 (75-84)	81 (77-85)	.5168
Specificity	87 (84-89)	84 (81-88)	89 (86-92)	.0724
Accuracy	84 (82-85)	82 (79-85)	85 (83-88)	.0907
High confidence	73 (71-75)	72 (69-75)	74 (71-77)	.496
IOA, κ	.55 (.47-.61)	.50 (.40-.58)	.59 (.49-.67)	†
Mucinous cystic neoplasms				
Sensitivity	57 (52-63)	50 (42-58)	64 (57-72)	.0094
Specificity	88 (86-90)	88 (86-91)	88 (86-91)	.9309
Accuracy	82 (80-84)	81 (78-83)	83 (81-86)	.1523
High confidence	44 (41-46)	44 (40-47)	44 (40-47)	.9567
IOA, κ	.32 (.22-.40)	.25 (.15-.32)	.38 (.25-.48)	†

	Overall	Refresher course	Self-learning	*P* value*
Cystic neuroendocrine tumor or solid pseudopapillary neoplasm				
Sensitivity	73 (68-78)	65 (57-74)	81 (74-88)	.0052
Specificity	93 (91-94)	91 (89-93)	94 (93-96)	.0198
Accuracy	90 (88-91)	87 (85-89)	92 (90-94)	.0006
High confidence	57 (55-59)	57 (54-60)	57 (54-60)	.9867
IOA, κ	.44 (.32-.54)	.32 (.22, 0.40)	.57 (.41-.69)	†
Pseudocyst				
Sensitivity	73 (62-85)	63 (46-81)	83 (70-97)	.0798
Specificity	97 (96-98)	96 (95-98)	98 (97-99)	.0664
Accuracy	96 (95-97)	95 (94-97)	97 (96-98)	.0179
High confidence	52 (50-55)	51 (48-55)	54 (50-57)	.8079
IOA, κ	.57 (.42-.67)	.46 (.27-.59)	.69 (.53-.79)	†
Serous cystadenoma				
Sensitivity	65 (58-71)	60 (51-69)	69 (60-78)	.1587
Specificity	97 (96-98)	96 (95-98)	98 (97-99)	.0148
Accuracy	93 (91-94)	91 (89-93)	94 (93-96)	.0164
High confidence	57 (55-60)	47 (44-51)	68 (65-71)	.0045
IOA, κ	.44 (.12-.61)	.33 (.13-.48)	.56 (.12-.79)	†

Values are % (95% confidence interval) unless otherwise defined.

IOA, Interobserver agreement.

*P value from χ^2 test.

†Not assessable.

TABLE 4.

Diagnostic accuracy, confidence, and IOA of early-career endosonographers for needle-based confocal laser endomicroscopy–guided diagnosis of pancreatic cystic lesions: comparison of phase 1 and phase 2 assessments

	Phase 1	Phase 2	*P* value
Mucinous vs nonmucinous			
Accuracy	85 (83-87)	89 (87-90)	.002
High confidence	76 (74-78)	83 (81-84)	<.001
IOA, κ	.57 (.48-.65)	.63 (.55-.70)	*
Intraductal papillary mucinous neoplasm			
Accuracy	84 (82-85)	84 (82-85)	1
High confidence	66 (64-68)	73 (71-75)	.003
IOA, κ	.61 (.52-.69)	.55 (.47-.61)	*
Mucinous cystic neoplasms			
Accuracy	82 (80-84)	82 (80-84)	.98
High confidence	41 (39-44)	44 (41-46)	.6
IOA, κ	.30 (.21-.39)	.32 (.22-.40)	*
Cystic neuroendocrine tumor or solid pseudopapillary neoplasm			
Accuracy	88 (86-89)	90 (88-91)	.07
High confidence	41 (39-43)	57 (55-59)	<.001
IOA, κ	.40 (.25-.51)	.44 (.32-.54)	*
Pseudocyst			
Accuracy	95 (94-96)	96 (95-97)	.08
High confidence	53 (50-55)	52 (50-55)	1

	Phase 1	Phase 2	*P* value
IOA, κ	.52 (.38-.63)	.57 (.42-.67)	*
Serous cystadenoma			
Accuracy	92 (90-93)	93 (91-94)	.37
High confidence	54 (51-56)	57 (55-60)	.51
IOA, κ	.47 (.18-.66)	.44 (.12-.61)	*

Values are % (95% confidence interval) unless otherwise defined.

IOA, Interobserver agreement.

*Not assessable.