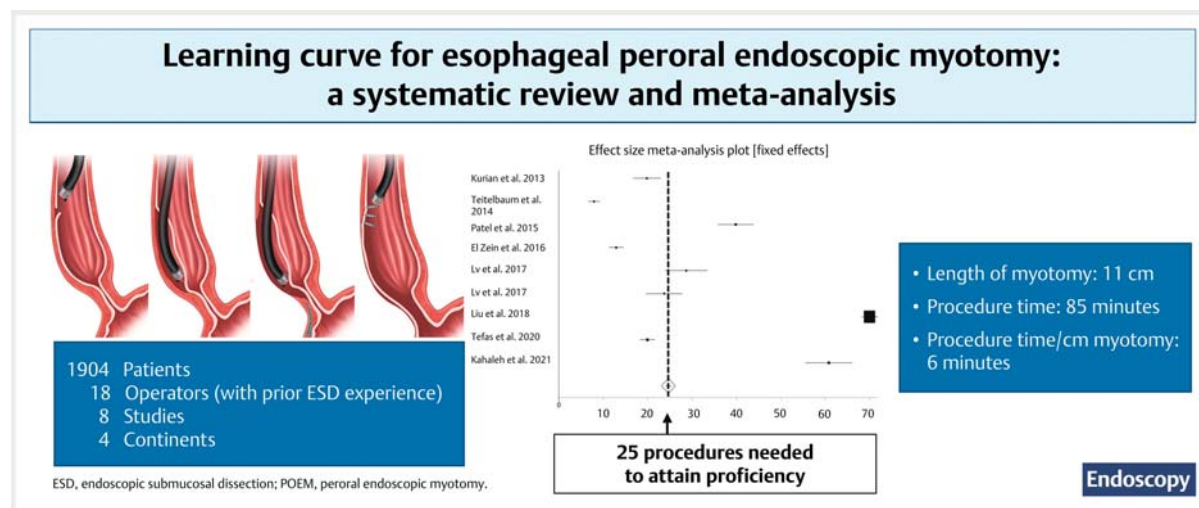


Learning curve for esophageal peroral endoscopic myotomy: a systematic review and meta-analysis

GRAPHICAL ABSTRACT



Authors

Srinivas R. Puli¹, Mihir S. Wagh², David Forcione³, Harishankar Gopakumar¹

Institutions

- 1 Department of Gastroenterology and Hepatology, University of Illinois College of Medicine at Peoria, Peoria, Illinois, United States
- 2 Division of Gastroenterology, University of Colorado School of Medicine, Aurora, Colorado, United States
- 3 Gastroenterology, Boca Raton Regional Hospital, Boca Raton, Florida, United States

Corresponding author

Harishankar Gopakumar, MD, FACP, Department of Gastroenterology and Hepatology, University of Illinois College of Medicine at Peoria, 530 NE Glen Oak Ave., Peoria, IL 61637, United States
harishankar.gopakumar@oshealthcare.org
hgopakumarmd@gmail.com

submitted 24.2.2022

accepted after revision 1.9.2022

published online 1.9.2022

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Endoscopy 2023; 55: 355–360

DOI 10.1055/a-1935-1093

ISSN 0013-726X

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Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

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ABSTRACT

Background and study aims Peroral endoscopic myotomy (POEM) is a minimally invasive endoscopic procedure for the treatment of achalasia and certain spastic esophageal motility disorders, delivering excellent results in experienced hands. However, this complex and technically challenging procedure requires advanced endoscopic skills. The aim of this study was to conduct a systematic review and meta-analysis of current data to evaluate the learning curve for POEM in new adopters of this technique.

Methods Electronic databases (PubMed, Embase, and Cochrane Library) from inception to November 2021 were searched for publications addressing the learning curve in POEM. Pooling was conducted by both fixed- and random-effects models. Secondary outcomes reviewed were clinical success defined by Eckardt score ≤ 3 when available and adverse events.

Results Eight studies involving 1904 patients met the inclusion criteria. In the pooled analysis, new adopters of

POEM attained proficiency at a mean of 24.67 procedures (95%CI 23.93 to 25.41). Once proficiency was achieved, the pooled total procedure time plateaued at a mean of 85.38 minutes (95%CI 81.48 to 89.28), the pooled mean procedure time per centimeter of myotomy was 6.25 minutes (95%CI 5.69 to 6.82), and the pooled mean length of myotomy was 11.49 cm (95%CI 10.90 to 12.08).

Conclusions Our analysis showed that new adopters of POEM with previous advanced endoscopy experience required about 25 procedures to attain proficiency. The average time for each procedure once proficiency was attained was about 85 minutes.

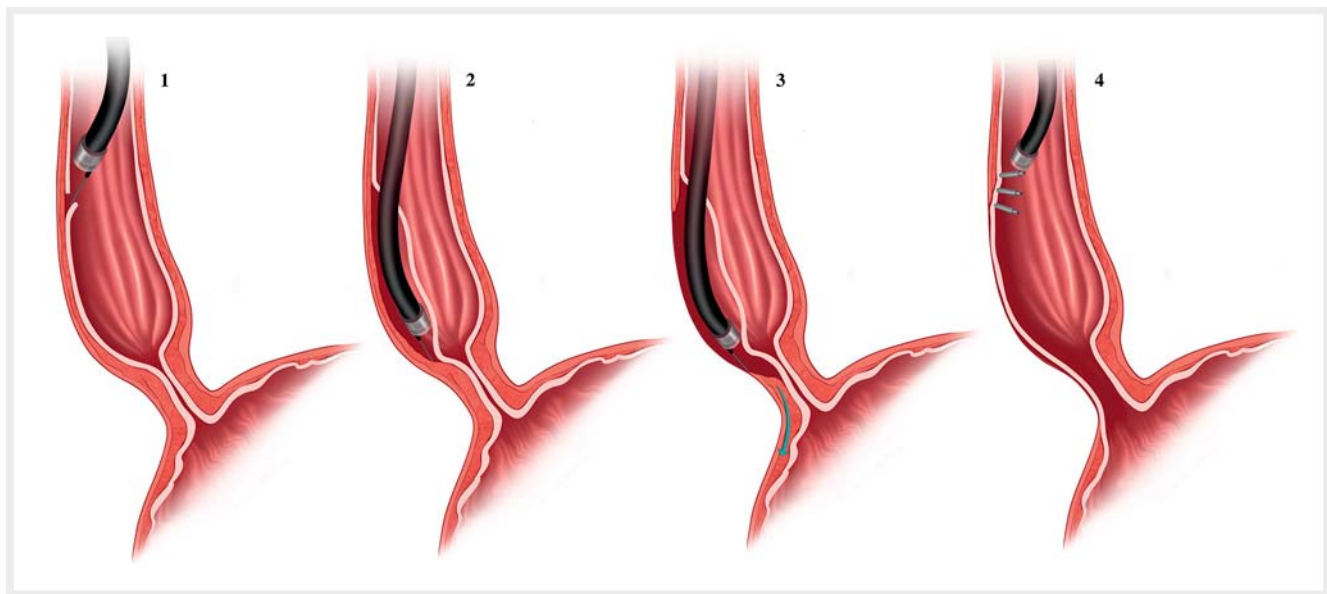
Introduction

Achalasia is a rare esophageal motility disorder characterized by aberrant peristalsis and insufficient relaxation of the lower esophageal sphincter. Dysphagia to both solids and liquids, regurgitation, retrosternal chest pain and weight loss are the most common presenting symptoms.

Durable symptom relief requires disruption of the muscle layer at the lower esophageal sphincter [1]. This can be achieved through pneumatic dilation, laparoscopic Heller myotomy (LHM), and more recently, peroral endoscopic myotomy (POEM). POEM has become the preferred treatment modality for the treatment of achalasia and various spastic esophageal motility disorders since its first description by Inoue et al. in 2010 [2–4]. POEM is a minimally invasive natural orifice transluminal endoscopic surgery procedure that consists of four broad sequential steps: mucosotomy (initial mucosal incision), submucosal tunneling, myotomy, and closure of the mucosal incision [4]. ▶ **Fig. 1** presents a schematic illustration of these four steps.

POEM is a challenging procedure to master and can cause potentially life-threatening adverse events. There is wide variability in the published literature on what is considered an ap-

propriate learning curve for POEM, ranging from 8 procedures according to Teitelbaum et al. [5] to 100 procedures according to Liu et al. [6]. There is also a lack of clarity on what parameters should be considered when evaluating the efficiency and mastery of this multistep procedure. The statistical methods used in studies also varies, and the retrospective nature of all studies and the difference in the parameters used by different authors to define the learning curve further limit homogeneity. Cumulative sum technique analysis was performed in the studies performed by Liu et al. [6], Patel et al. [7], Kahaleh et al. [8], and Lv et al. [9]. Liu et al. evaluated the learning curve for POEM based on a primary outcome that was a composite of technical failure and adverse events [6], whereas all other studies have focused almost entirely on plateauing of procedure time as a measure of proficiency [4, 5, 7–11]. Based on their evaluation, Liu et al. concluded that 100 cases were required to decrease the risk of technical failure, adverse events, and clinical failure (which was the definition of the learning curve) [6]. The authors argued that the feasibility and safety of a procedure are closely associated with technical failure, which therefore should be the main end point determining proficiency. In their study, Liu et al. noticed that technical proficiency, if defined by plateauing of procedure time could be achieved at about 70 cases. How-



▶ **Fig. 1** Schematic illustration of the four steps of peroral endoscopic myotomy. 1. Mucosotomy. 2. Submucosal tunneling. 3. Myotomy. 4. Closure of the mucosal incision.

ever, as POEM is a multistep procedure, inconsistencies occur when total procedure time is used as a surrogate of proficiency. In their retrospective analysis of 60 patients who underwent POEM at Johns Hopkins hospital by a single interventional gastroenterologist, El Zein et al. observed that total operative time, mucosal entry time, submucosal tunneling time, and time for closure of mucosal entry decreased significantly with experience, whereas endoscopic myotomy time did not [10]. However, the authors did mention that when procedure time per centimeter of myotomy was taken into account, the learning rate was 11 cases with a learning plateau of 10 min/cm [10]. Many of the data on outcomes are from large-volume centers where the learning curve represented the personal experience of one experienced endoscopist who was already proficient in advanced interventional endoscopic procedures or the experience of an expert foregut surgeon proficient in LHM and flexible endoscopy [4, 8].

This systematic review and meta-analysis aimed to pool the results of published data on esophageal POEM in terms of the learning curve involved in attainment of proficiency.

Methods

The study is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

Search methodology

A literature search was conducted using the electronic databases MEDLINE, PubMed, Ovid, Cochrane library (Cochrane Central Register of Controlled Trials and Cochrane Database of Meta-Analysis), EMBASE, ACP Journal Club, Database of Abstracts of Reviews of Effects (DARE), from January 1974 to November 2021, to identify studies addressing the learning curve for POEM. Keywords used were “POEM,” “Peroral Endoscopic Myotomy,” “Achalasia,” and “Learning Curve.” The retrieved studies were carefully examined to exclude potential duplicates or overlapping data.

Study eligibility

Published studies were eligible if they reported a learning curve for POEM with data and discussion on methodology. Articles were excluded if they were not in the English language. Studies in animal models, editorials, and comments were excluded. Studies matching the inclusion criteria were retrieved as full-text articles and reviewed independently by two authors (H.G., S.R.P.). Differences were resolved by discussion to reach agreement.

Data extraction and quality assessment

The following data were independently abstracted by two authors (H.G., S.R.P.) into a standardized form: study characteristics (primary author, period of study, year of publication, and country of the population studied), study design, baseline characteristics of the study population (number of patients en-

rolled, patient demographics), intervention details (number of POEM procedures, indications, length of procedure including total and subdivisions when available, number of operators, specialty and experience of the operator), and outcomes (learning curve, definition of learning, complications, Eckart scores). Differences were resolved by discussion. The risk of bias was rated for each study by two authors independently, using the Cochrane criteria for randomized controlled trials.

Outcomes evaluated

Pooled estimates of the number of procedures required to attain proficiency, pooled estimates of the total procedure time once proficiency was achieved, and mean procedure time per centimeter of myotomy were analyzed. Secondary outcomes reviewed were clinical success defined by Eckardt score ≤ 3 when available and adverse events.

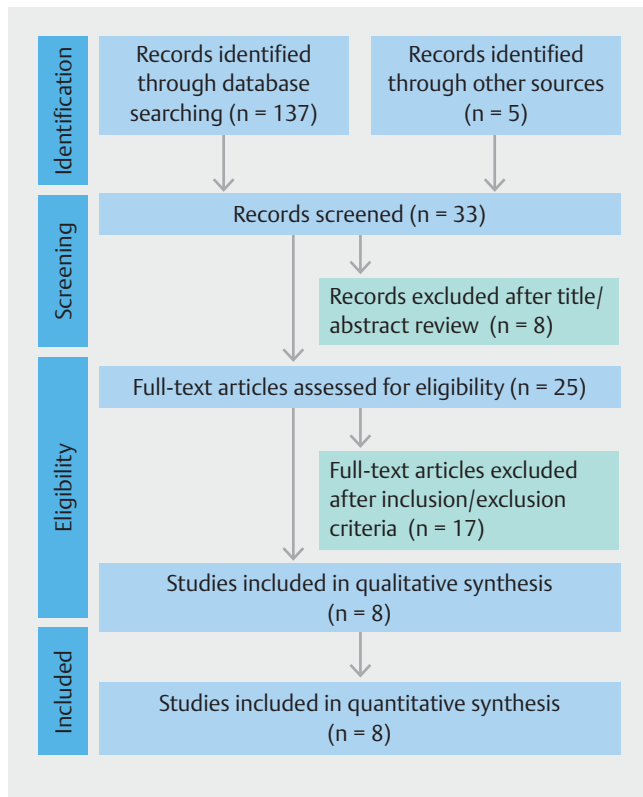
Statistical analysis

The meta-analysis was performed by calculating pooled proportions. Individual study proportions were transformed into a quantity using the Freeman–Tukey variant of the arcsine square-root transformed proportion. The pooled proportion was calculated as the back-transform of the weighted mean of the transformed proportions, using inverse arcsine variance weights for the fixed-effects model and DerSimonian–Liard weights for the random-effects model. Forest plots were drawn to show the point estimates for each study in relation to the summary of pooled estimate. The width of point estimates on the forest plots indicates the assigned weight to that study. The effects of publication and selection bias on the summary estimates were tested by both the Harbord–Egger bias indicator [12] and Begg–Mazumdar bias indicator [13]. Funnel plots were constructed to assess potential publication bias using the standard error and diagnostic odds ratio [14]. Statistical analysis was performed using the software Microsoft Excel 19 [15].

Results

After careful review and evaluation, eight articles were found that addressed the question of a learning curve for achieving proficiency in the performance of POEM [4–11]. The PRISMA flow chart describing the details of the review process is presented in ► Fig. 2. All included studies are available as full-text articles. All pooled estimates were calculated by the fixed-effects model.

The total sample size was 1904 patients who underwent a total of 1904 POEM procedures. Overall, 51% of patients were men and 49% were women. Five of the studies reported on POEM procedures performed by gastroenterologists, whereas the remaining three studies reported on POEM procedures performed by surgeons. All five of the studies on POEM performed by gastroenterologists involved a single operator, whereas the three performed by surgeons involved multiple operators (2–7), including new trainees. The indication for POEM procedure was achalasia in 98% of patients. Basic study characteristics are represented in ► Table 1.



► **Fig. 2** Flow chart of study selection according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Pooled analysis showed that the mean number of POEM procedures at which a new adopter attained proficiency was 24.67 (95%CI 23.93 to 25.41). A forest plot showing individual study estimates and the pooled analysis is shown in ► **Fig. 3**.

Harbord–Egger bias indicator [12] was calculated as 13.88 (95%CI –23.95 to 51.72; $P = 0.41$) showing there was no publication bias. ► **Fig. 4** represents the funnel plot assessing the publication bias for mean number of POEM procedures at which a new adopter attained proficiency.

The total procedure time plateaued at a pooled mean of 85.38 minutes (95%CI 81.48 to 89.28) once proficiency was achieved. At this stage, the pooled mean procedure time per centimeter of myotomy was 6.25 minutes (95%CI 5.69 to 6.82) and the pooled mean length of myotomy was 11.49 cm (95%CI 10.90 to 12.08). The pooled estimates calculated using fixed- and random-effects model were similar.

Discussion

POEM is a relatively recent, minimally invasive endoscopic technique for the treatment of achalasia and certain spastic esophageal disorders [1]. Multiple studies have shown POEM to be safe and effective with results comparable to LHM [2, 16–18]. Following its introduction by Inoue et al. in 2010 [2], there has been a rapid adoption of this procedure worldwide, with POEM becoming part of many therapeutic endoscopy programs. However, achalasia is a rare condition and POEM is a complex procedure requiring advanced endoscopy skills. There is wide variability in currently available data on what is considered to be an appropriate learning curve for attainment of proficiency and mastery of this technique [4, 11]. Early adopters of POEM had extensive prior experience in advanced endoscopy and these procedures were performed at centers with high volumes. With the availability of POEM training in advanced endoscopy fellowship programs to endoscopists with minimal or no prior experience in endoscopic submucosal dissection (ESD), there is a need to formalize training with a comprehensive understanding of the learning curve to ensure quality. There should be an emphasis on POEM training to proficiency rather than just focusing on procedure numbers, with trainers evaluating POEM skills and providing ongoing feedback to trainees [19–25].

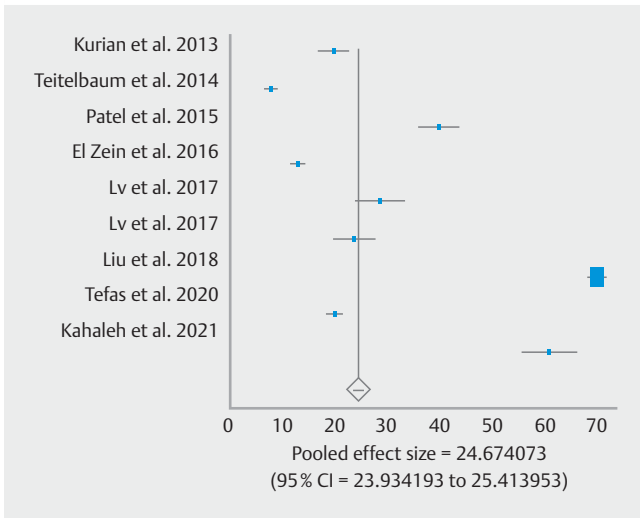
Our meta-analysis of studies evaluating the learning curve of POEM published over the past 10 years included a total of 1904 patients who underwent a total of 1904 procedures. In our analysis, the mean number of procedures required to attain proficiency was 25. This result is very similar to the results observed in an animal model study by Hernández Mondragon et

► **Table 1** Basic study characteristics.

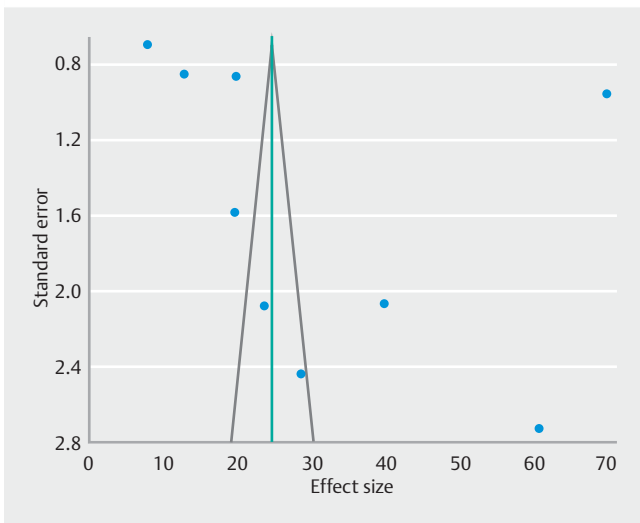
Number	Author	Year	POEMS, n	No. of operators	Prior operator experience*	Type of study
1	Kurian et al. [4]	2013	40	3	LHM, POEM in lab	Retrospective
2	Teitelbaum et al. [5]	2014	36	2	LHM, POEM in lab	Retrospective
3	Patel et al. [7]	2015	93	1	ESD	Retrospective
4	El Zein et al. [10]	2016	60	1	POEM in lab	Retrospective
5	Lv et al. [9]	2017	68	1	ESD	Retrospective
6	Liu et al. [6]	2018	1346	7	ESD	Retrospective
7	Tefas et al. [11]	2020	136	1	Not specified	Retrospective
8	Kahaleh et al. [8]	2021	125	1	ESD	Retrospective

ESD, endoscopic submucosal dissection; LHM, laparoscopic Heller myotomy; POEM, peroral endoscopic myotomy.

* POEM in lab includes lab simulation, live porcine, and human cadaver models.



► **Fig. 3** Forest plot showing pooled estimates of mean number of peroral endoscopic myotomy (POEM) procedures required to attain proficiency. The study by Lv et al. reported on the POEM learning curve for two separate gastroenterologists, which have been analyzed separately.



► **Fig. 4** Funnel plot of publication bias on number of procedures required to attain proficiency.

al., which found that the number of procedures to attain mastery of POEM when performed on a swine model was 26 [26]. Proficiency in all but one (Liu et al. [6]) study was primarily defined by the number of procedures at which plateauing of procedure time was observed. Our analysis showed that the mean total procedure time, once proficiency was attained, was 85 minutes. Three studies evaluated the procedure times subdivided into their component steps [4, 9, 10]. Analysis showed that the mean procedure time calculated per centimeter of myotomy was 6 minutes. There is uncertainty about what other

parameters should be considered when evaluating proficiency in addition to time to complete a POEM procedure. This information will help to ensure appropriate mentorship programs, allow endoscopy units to allot appropriate time slots for POEM procedures, and establish guidelines for POEM training. To our knowledge, this is the first systematic review and meta-analysis evaluating currently available data on the learning curve for POEM.

There are a few limitations to this study. All studies included were limited by the retrospective nature of the data. Out of the total of 1904 patients in the sample, 1346 were from one study by Liu et al. [6]. The results of that study could have disproportionate weighting to the conclusions of this meta-analysis. However, a strong feature of performing a meta-analysis is calculating a weighted average. This weighted average gives a realistic estimate. Being the largest study to date addressing the learning curve for POEM, it would also not be appropriate to exclude it from this analysis. In addition, it is important to note that in all the studies evaluating the learning curve of POEM, the operators had extensive previous experience in advanced endoscopic techniques including ESD, and were often pioneers in their countries. There is a paucity of data evaluating the learning curve for POEM in endoscopists with limited previous experience in advanced endoscopic procedures, such as fellows and surgical trainees. In addition, most studies outline the personal journey of one endoscopist learning POEM. However the advantage of prior experience in someone pioneering a new technique should also be weighed against the advantage of more recent training that benefits from more than a decade of cumulative experience gained, especially if from a well-recognized, advanced endoscopy training program with adequate exposure to third space endoscopy. We acknowledge that total procedure times are not necessarily the best indicator of achievement of proficiency in performing a certain procedure, and variations could be multifactorial, including individual protocols at various institutions, patient characteristics, anatomical considerations, and selection of endoscopy tools. Achievement of clinical success with a reduction in adverse events may be a better marker for the learning curve for POEM. The lack of information on these outcomes limited our choice of variables to evaluate in the current study and therefore restricted our ability to adequately evaluate the learning curve for POEM.

Conclusions

The success of POEM over the past decade has encouraged wider adoption of this technique including by trainees in many advanced endoscopy fellowship programs where training in POEM is offered. Our analysis showed that new adopters of POEM with prior expertise in advanced endoscopy may require about 25 procedures to attain proficiency, with an average time of 85 minutes for each procedure once proficiency is attained. This information can assist in the development of POEM training programs, planning endoscopy time slots, and proficiency assessment. Further research is needed to determine the number of procedures and parameters to be considered in the evaluation of proficiency in adopters of POEM with limited prior ad-

vanced endoscopy experience. Ensuring continued proficiency after initial training will also be pertinent, especially if practicing in low-volume centers in order to assure high-quality patient care.

Competing interests

M. Wagh is a consultant for Olympus, Boston Scientific, Medtronic, Fujifilm, Incyte, and ConMed, and receives research support from Steris/US Endoscopy. S.R. Puli, D. Forcione, and H. Gopakumar declare that they have no conflict of interest.

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