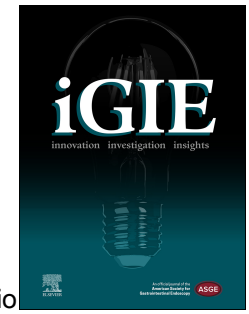


Implementation of Endoscopic Submucosal Dissection in Europe: Survey after ten ESD Expert Training Workshops 2009 – 2018

Tsuneo Oyama, MD PhD, Naohisa Yahagi, MD PhD, Thierry Ponchon, MD PhD, Tobias Kiesslich, PhD, Andrej Wagner, MD PhD, Takashi Toyonaga, MD PhD, Toshio Uraoka, MD PhD, Akiko Takahashi, MD, Alexander Ziachehabi, MD, Daniel Neureiter, MD PhD, Maria Fuschlberger, Franz Schachinger Mag., Hans Seifert, MD PhD, Georg Kaehler, MD PhD, Alexandr Mitrakov, MD, Sergey V. Kantsevoy, MD PhD, Helmut Messmann, MD PhD, Juergen Hochberger, MD PhD, Frieder Berr, MD PhD, the ESD Workshop Training Group

PII: S2949-7086(23)00096-1

DOI: https://doi.org/10.1016/j.igie.2023.08.004

Reference: IGIE 81

To appear in: *iGIE*

Received Date: 31 May 2023

Revised Date: 13 July 2023

Accepted Date: 14 August 2023

Please cite this article as: Oyama T, Yahagi N, Ponchon T, Kiesslich T, Wagner A, Toyonaga T, Uraoka T, Takahashi A, Ziachehabi A, Neureiter D, Fuschlberger M, Mag. FS, Seifert H, Kaehler G, Mitrakov A, Kantsevoy SV, Messmann H, Hochberger J, Berr F, the ESD Workshop Training Group, Implementation of Endoscopic Submucosal Dissection in Europe: Survey after ten ESD Expert Training Workshops 2009 – 2018, *iGIE* (2023), doi: https://doi.org/10.1016/j.igie.2023.08.004.

Implementation of Endoscopic Submucosal Dissection in Europe: Survey after ten ESD Expert Training Workshops 2009 – 2018

Tsuneo Oyama, MD PhD[1], Naohisa Yahagi, MD PhD[2], Thierry Ponchon, MD PhD[3], Tobias Kiesslich, PhD[4,5], Andrej Wagner, MD PhD[4], Takashi Toyonaga, MD PhD[6], Toshio Uraoka, MD PhD[7], Akiko Takahashi, MD [1], Alexander Ziachehabi, MD[8], Daniel Neureiter, MD PhD[9], Maria Fuschlberger[4], Franz Schachinger Mag. [10], Hans Seifert, MD PhD[11], Georg Kaehler, MD PhD[12], Alexandr Mitrakov, MD[13], Sergey V. Kantsevoy, MD PhD[14], Helmut Messmann, MD PhD[15], Juergen Hochberger, MD PhD[16], Frieder Berr, MD PhD[4,5]*, and the ESD WORKSHOP TRAINING GROUP[17]

[1]..Department of Endoscopy, Saku Central Hospital Advanced Care Center, Saku, Nagano prefecture, Japan
[2]..Division of Research and Development for Minimally Invasive Treatment, Cancer Center, Keio University School of Medicine, Shinjuku-ku, Tokyo-to,Tokyo, Japan
[3]..Specialités Digestives, Hôpital Edouard Herriot, Medical University of Lyon, Lyon, France
[4]..Department of Internal Medicine I, University Hospital, Paracelsus Medical University, Salzburg, Austria
[5]..Center for Physiology, Pathophysiology and Biophysics, Institute of Physiology and Pathophysiology, Paracelsus Medical University, Salzburg, Austria
[6]..Department of Endoscopy, Kobe University Hospital, Kobe, Kobe, *Hyōgo* prefecture, Japan
[7]..Department of Gastroenterology and Hepatology, Gunma University Hospital, Maebashi, Gunma prefecture, Japan
[8]..Endoscopy Center, Kepler University Hospital, Linz, Austria
[9]..Institute of Pathology, University Hospital, Paracelsus Medical University, Salzburg, Austria
[10]..Veterinary Practice, 4950 Altheim, Austria
[11]..Department of Medicine–Gastroenterology, University Hospital Oldenburg, Oldenburg, Germany
[12]..Endoscopy Center, Surgical Clinic, University Hospital Mannheim, University Heidelberg, Germany
[13]..Endoscopy Unit, Cancer Hospital, Privolzhskiy Research Medical University, Nizhniy Novgorod, Russian Federation
[14]..Institute for Digestive Health and Liver Disease, Mercy Medical Center, University of Maryland, Baltimore, USA
[15] ..Department of Gastroenterology, University Hospital Augsburg, Augsburg, Germany
[16]..Department of Gastroenterology, Vivantes Hospital Berlin-Friedrichshain, Berlin, Germany
[17]..ESD Workshop Expert Training Group listed in Addendum, Supportive Information 1

***Corresponding author**

Frieder BERR, MD
Department of Internal Medicine I, University Hospital Salzburg, Paracelsus Medical University, Muellner Hauptstrasse 48, 5020 Salzburg, Austria
Tel. ++43 5 7255 25401, Fax ++43 5 7255 25599, e-mail frieder.berr@pmu.ac.at

Running Head
Survey of ESD implementation

Implementation of Endoscopic Submucosal Dissection in Europe: Survey after ten ESD Expert Training Workshops 2009 – 2018

Tsuneo Oyama, MD PhD[1], Naohisa Yahagi, MD PhD[2], Thierry Ponchon, MD PhD[3], Tobias Kiesslich, PhD[4,5], Andrej Wagner, MD PhD[4], Takashi Toyonaga, MD PhD[6], Toshio Uraoka, MD PhD[7], Akiko Takahashi, MD [1], Alexander Ziachehabi, MD[8], Daniel Neureiter, MD PhD[9], Maria Fuschlberger[4], Franz Schachinger Mag. [10], Hans Seifert, MD PhD[11], Georg Kaehler, MD PhD[12], Alexandr Mitrakov, MD[13], Sergey V. Kantsevoy, MD PhD[14], Helmut Messmann, MD PhD[15], Juergen Hochberger, MD PhD[16], Frieder Berr, MD PhD[4,5]*, and the ESD WORKSHOP TRAINING GROUP[17]

[1]..Department of Endoscopy, Saku Central Hospital Advanced Care Center, Saku, Nagano prefecture, Japan
[2]..Division of Research and Development for Minimally Invasive Treatment, Cancer Center, Keio University School of Medicine, Shinjuku-ku, Tokyo-to,Tokyo, Japan
[3]..Specialités Digestives, Hôpital Edouard Herriot, Medical University of Lyon, Lyon, France
[4]..Department of Internal Medicine I, University Hospital, Paracelsus Medical University, Salzburg, Austria
[5]..Center for Physiology, Pathophysiology and Biophysics, Institute of Physiology and Pathophysiology, Paracelsus Medical University, Salzburg, Austria
[6]..Department of Endoscopy, Kobe University Hospital, Kobe, Kobe, *Hyōgo* prefecture, Japan
[7]..Department of Gastroenterology and Hepatology, Gunma University Hospital, Maebashi, Gunma prefecture, Japan
[8]..Endoscopy Center, Kepler University Hospital, Linz, Austria
[9]..Institute of Pathology, University Hospital, Paracelsus Medical University, Salzburg, Austria
[10]..Veterinary Practice, 4950 Altheim, Austria
[11]..Department of Medicine–Gastroenterology, University Hospital Oldenburg, Oldenburg, Germany
[12]..Endoscopy Center, Surgical Clinic, University Hospital Mannheim, University Heidelberg, Germany
[13]..Endoscopy Unit, Cancer Hospital, Privolzhskiy Research Medical University, Nizhniy Novgorod, Russian Federation
[14]..Institute for Digestive Health and Liver Disease, Mercy Medical Center, University of Maryland, Baltimore, USA
[15] ..Department of Gastroenterology, University Hospital Augsburg, Augsburg, Germany
[16]..Department of Gastroenterology, Vivantes Hospital Berlin-Friedrichshain, Berlin, Germany
[17]..ESD Workshop Expert Training Group listed in Addendum, Supportive Information 1

***Corresponding author**

Frieder BERR, MD
Department of Internal Medicine I, University Hospital Salzburg, Paracelsus Medical University, Muellner Hauptstrasse 48, 5020 Salzburg, Austria
Tel. ++43 5 7255 25401, Fax ++43 5 7255 25599, e-mail frieder.berr@pmu.ac.at

Running Head
Survey of ESD implementation

Author's contribution

The work examines the outcome (= implementation of ESD) of 10 years of intercontinental transfer of novel endo-surgical skills (ESD) and endo-diagnostic competence (indication for ESD vs. alternative resection procedures) to Western endoscopy experts (topic review Oyama T. et al., 2015, World J Gastroenterol).

1. **Conception** (OT 35%, YN 15%, BF 10%, KT 10%, SF 10%, FM 5%, ND 5%, KS 5%, MA 5%) & **design** (PT, TT, UT, TA, WA, ZA, SH, KG, MH, HJ, each 10%).
   Acquisition of data (ESD Workshop Training Group; SH, ZA, MA, BF, each 1.35%).
   Analysis of Data (BF 40%, KT 30%, WA 20%, ND 10%).
   Interpretation of Data (OT 20%, YN 10% BF 20%, KT 10%, WA 10%, SH 10%, HJ 20%).
2. **Drafting and revising**: (BF 30%, OT 20%, YN 10% KT 15%, HJ 15% [drafting], all others 10% [revising])
3. **Final approval of work** (manuscript) by the 19 authors and the entire ESD Workshop Training Group.
4. **Agreement to be accountable** for the work by all authors (as related to their contributions).

Abstract

Background and aims: Transfer of ESD technique for early gastrointestinal cancer from Japan requires expert-supervised experimental training before unsupervised implementation of clinical ESD.
Aims: To evaluate unsupervised implementation of ESD-intention-to-treat (-ITT).

Methods: ESD Workshops (in-vivo porcine model) lasted 3.3 days including one day theory for 177 participants from 135 *Western* referral centers. A questionnaire was sent to the senior participant of all 135 centers.
Design: Cross-sectional questionnaire survey.
Main outcome measurements: performance, organ distribution, severe adverse events of ESD-ITT.

Results: Feedback was received from 113 centers (84%), i.e. 73 (54%) ESD centers and 40 centers (30%) with zero ESD; 10 (7%) had published ESD; no feedback from 12 (9%) centers with unknown status. Altogether, 83 centers (61.5%) perform ESD: 21 (16%) had >150 ESD (professional category), 33 (24%) had 31-150 ESD (competent category), and 29 (21.5%) had ≤ 30 ESD (initial learning category). Most implemented ESD centers (91%, 72 of 79) were analyzed: Centers on initial learning (420 ESD) compared to centers with >30 ESD (5676 ESD) performed en-bloc ESD in 64% vs. 84%, hybrid-ESD in 26% vs.11% and piecemeal-EMR in 10% vs. 5.2%. Majority of ESD (66-68%) were in colorectum, overall with low risk (30-day mortality 0.03%, surgical repair 3.5% vs. 1.7%) and satisfactory outcome (oncosurgery 7.4% vs. 5.2%, local recurrence 1.5% vs. 0.3%).

Conclusions: Beyond guideline recommendations, unsupervised implementation of ESD was successful in colorectum with step-up approach. Now, Western ESD centers have to aim for professional (i.e. >80%) curative ESD.

Keywords
ESD implementation, ESD training workshop, adverse events of ESD, ESD outcome

Introduction

To transfer endoscopic submucosal dissection (ESD) of early gastrointestinal (GI) cancer from Japan to Europe requires expert-supervised experimental training of experienced endoscopists, before they can implement human ESD in Europe. In 2008, a structured approach had been proposed by Japanese experts, including observation of expert ESD procedures and performance of five ESD procedures under supervision of leading Japanese experts in an *in vivo* experimental model before starting to perform unsupervised ESD procedures on patients [1, 2]. From 2009 to 2018, Paracelsus Medical University (PMU) Salzburg had set up 10 such annual ESD EXPERT TRAINING WORKSHOPS (2.3 days hands-on plus 1 day theory seminar) to allow for an average of 4–5 supervised ESD procedures per participant in a porcine model [3], complemented with a third day (UPDATE seminar) on clinical case studies and theory presented by the Japanese and Western experts. The strategy of this ESD training program, how to implement and advance ESD centers in Western countries, has been detailed in a topic article [2].

Objective of the questionnaire survey: To evaluate in the participating centers the extent and severe adverse events (sAE) of unsupervised implementation of clinical ESD intention-to-treat (ESD-ITT) – that is any resection planned and started as en-bloc ESD.

Background

En-bloc ESD allows precise histopathologic staging of tumor category, grading, and resection margin status and provides cure of early gastrointestinal (GI) cancer [4-9]. Japan Gastrointestinal Endoscopy Society (JGES) has validated classical criteria of histopathologic curative ESD (zero risk of metastasis) in the entire GI tract, and expanded criteria (risk <4% of regional metastasis) in stomach and esophagus [7, 10, 11]. Endoscopic classifications (macroscopic, microsurface and microvessel types) predict with high accuracy (> 85-90%) premalignant and malignant lesions in the early stage and define indications for ESD vs. piecemeal endoscopic mucosal resection (PM-EMR) vs. surgery with lymphadenectomy [12-16]. Professional ESD centers in Japan achieve >80% curative resection (CR) of ESD [4, 10, 11].

Hence, implementation of ESD requires two learning curves for: 1) accurate endoscopic prediction of pT linked tumor category using image-enhanced endoscopy (IEE) which is the basis for correct differential indication of ESD vs. surgery with lymphadenectomy, - and 2) highly skilled endoscopic electrosurgical resection. In Japan, ESD has rapidly been adopted through thoroughly designed clinical training system based on direct day-to-day individual supervision of the learners by the top Japanese experts. Such expertise was not yet available in Europe in the year 2009 [1]. European interventional endoscopists had to master the learning curve for ESD in an unsupervised fashion [1, 2].

Methods

Ethics Committee

For the questionnaire survey, ethics committee approval was not required, because the feedback of participating 135 centers on implementation of clinical ESD has been used for anonymized descriptive analyses, and all 73 centers providing quantitative data have approved the manuscript and listing of the senior participant by name and affiliation. Each annual ESD Workshop has been a priori approved by the governmental Ethics Committee and Animal Ethics Committee (BMWF 66.012/0006-II/10b/2009 through 66.019/0029-WF/V/3b/2018), was led by veterinarian teams and monitored for compliance with European regulations for protection of animals in experimental research. All ESD Workshop and Update events have been endorsed by the European Society of Gastrointestinal Endoscopy (ESGE) including the ESD LIVE events [17], and since 2016 for educational credits by European Union of Medical Specialists (https://eaccme.uems.eu).

Description of the annual ESD Training Workshop and Update

The basic format of the hands-on training course on piglets (20–25 kg body weight) in general anesthesia has been described in detail - see [3], and for detailed program supporting information 2. All 10 experimental hands-on workshops were held at the anatomic training facilities of the PMU in Salzburg, Austria and included an introductory seminar (2.5 hrs, on course structure and techniques) on the day of arrival, two full days of hands-on training (two 4.5 hrs sessions per day), and the clinical UPDATE seminar on the third day (open to the general audience) with case

studies and interactive presentations by the experts (including 4 ESD LIVE every year since 2012). From 2009 to 2013, there were six working stations - two each for hook-~® [6], dual-~® [18], and hybrid-knife® [19, 20] - and from 2014 to 2018 there were eight working stations – two each for hook-J ~®, dual-J ~® (Olympus Europe, Hamburg, DE), hybrid ~® (ERBE Elektromedizin GmbH, Tübingen, DE), and flush knife BT® [21] (FUJIFILM Europe GmbH, Ratingen, DE). Supervision and individualized instruction on the ESD technique was given by three, respectively four top experts from Japan and the same number of Western experts at the parallel training stations. In brief, participants performed hands-on training in teams of three taking turns every 20 min and rotating to another working station after every 60 min. Hence, each participant passed through all 8 training stations and tutors per day. Reference material was an annually updated syllabus on the endoscopic analysis of early GI neoplasias, differential indications (EMR vs. ESD vs. resective surgery), and details on ESD techniques, electrosurgical settings, supply material, training steps, risks for AE and management (under www.early-cancer.eu, pass word on request from the corresponding author) and, since 2014, an atlas on endoscopic analysis and differential indication (according to JEGS) for early GI neoplasias [13].

Participants

All candidates were highly EMR-experienced senior endoscopists from major referral centers, and had to state prior experience with human ESD (if any) in order to match the training teams of each 3 participants with comparable experience. In accordance with an ESGE board member (Th.P.), participating candidates were chosen based on best interventional experience as well as geographical distribution and suitability of their centers.

The ESD Expert Training Workshops 2009-2018 provided 210 trainee slots (5 x 18 (2009-2013) + 5 x 24 (2014-2018)) for 208 trainee participants (& two cancellations). Total of 177 trainees have participated, 27 trainees participated two times and 2 participated three times. The 177 participants came from 144 centers (29 centers had 2 participants and two centers 3 participants). Nine centers (6%) were excluded from analysis because of loss to follow-up of the participant, i.e. 3 in USA, 1 each in England, Argentine, Reunion (FR), New Zealand, Singapore, and Morocco. Altogether, 135 centers were surveyed: 133 from Europe and Mediterranean Near East, and two from USA.

Course Feedback of Participants. In all 10 Workshops and Updates, participants have rated the teaching excellent by the leading ESD experts from Japan and by Western experts and the course very helpful to implement the novel ESD procedure in their hospitals (Supporting information 3).

Questionnaire

A structured questionnaire including the recommended ESD center structure ([2], Supporting information 4) was e-mailed to the *senior participant* of all 144 centers in March 2018 (and in May 2019 for Workshop 2018), to obtain information on implementation of ESD-ITT. The senior participant received a reminder after one month, and by phone after 2 months.

Statistical Analysis

Altogether 73 centers responded with completed questionnaire data, one (Institute Paoli Calmettes, pre-established ESD center [22]) was excluded, and 72 were included in statistical analysis. Overall mortality was calculated on total number of cases per total number of ESD reported by the 72 centers. All other parameters are given as percentage of total ESD number per center, analyzed for mean ± SE and for statistical differences using one-way ANOVA with Bonferroni's adjustment.

For categorical analysis of the supply network of ESD centers, all active ESD centers were categorized as proposed by Oyama et al. [2]: "initial learning category" for the first 30 unsupervised ESD-ITT, 'competent performance category' for 31 – 150 ESD-ITT, and 'professional category' after 150 ESD-ITT. In addition, any human ESD experience of the senior participant prior to this course was accordingly categorized.

Results

Survey of centers. Of all 135 centers, feedback had been obtained by the senior participant for 113 (84%), i.e. 73 responding active ESD centers (54%) and 40 centers (30%) with zero ESD performed. No feedback had been received from 22 centers (16%), i.e. 12 without ESD reputation nor publication and 10 centers with published ESD (6 in professional category in Augsburg, Berlin, Istanbul-Kocaeli, Lyon, Marseille, Porto [22-27] and 4 in competent category in Besançon, Grenoble, Liège, Leiden [28-30]) (Fig. 1A). Total of 83 centers (61%) had been performing ESD,

29 on initial, 33 on competent, and 21 on professional category. The centers of ESD workshop trainees have implemented an ESD supply network (Fig. 1B) – other ESD centers in Europe that had not participated are not shown [31-41] ([31] current affiliation St. Petersburg).

Centers with implementation of ESD. Categorical analysis shows 79 implemented and 4 pre-established ESD centers (Fig. 1C). In years 2017-2018, the four pre-established professional centers had delegated two participants on zero experience (Berlin, Istanbul-Kocaeli) [24, 25] or had participated with two advanced experts [22, 27]. The 29 centers on initial learning (≤30 ESD) were started by trainees without prior ESD experience (<10 ESD). The 33 centers on competent category (31-150 ESD) were implemented by senior participants on zero or initial (≤30 ESD) prior experience (n=29) or competent (n=4) prior experience. Trainees on zero or initial prior experience have set up 12 of 17 professional category centers, and trainees on competent ESD prior experience (n=5) contributed to the other five (Augsburg, Lodz, Mannheim, Nizhniy Novgorod, Poznan). Hence, 70 (89%) of the 79 started or implemented ESD centers had zero or only initial ESD prior experience.

Performance of ESD during Implementation. The survey data includes 72 responding centers only, and none of the pre-established or non-responding published centers. The survey of years 2018-2019 provides a cross-sectional overview on unsupervised implementation of ESD by former participants of this expert training course. All questionnaires stated the data is based on ESD indications according to JGES (Tab 1 in [2]), histologic assessment for grading, extension and invasion of early cancer, and a prospective data register for ESD indication, performance, outcome and follow-up. The annual ESD volume during the past year was 30±5 for competent and 77±18 ESD for professional category centers. Performance of ESD is compared between 29 centers on initial learning (n = 420 ESD, follow-up 18±3 mo), 29 competent (n = 2104 ESD, follow-up 49±6 mo), and 14 professional category centers (n = 3572 ESD, follow-up 82±5 mo) by subgroup analysis with significance levels shown in Fig. 2.

The majority (mean 66 - 72%) of all ESD-ITT were performed on colorectal neoplasias (46±3% malignant), irrespective of the performance category. Nevertheless, some step-up approach is apparent from the data (Fig. 2A): beginners

performed on average 57.5% rectal ESD, 28% gastric, 9% colonic, and 5.5% esophageal ESD. Competent and professional category centers show stepwise less rectal (mean 53% and 39%) and gastric ESD (20% and 14%), and up to threefold more colonic (15% and 32%; P<0.005) and esophageal ESD (13% and 15%). Some of these centers implemented ESD mainly or exclusively with colorectal step-up approach [42-45].

Mean rate of en-bloc ESD was low (64%) for centers on initial learning, but significantly higher on competent (82%) and on professional category (88%)(Fig. 2B). Beginners frequently (26%) used hybrid-ESD as compared to competent (13%; P<0.05) and professional category (7.5%; P<0.02), and conversion to piecemeal EMR in 10% vs. 6% and 4.5%.

Adverse outcome of ESD-ITT. Even without supervision during the initial learning curve, clinical ESD has been implemented by course participants with low risk and satisfactory oncological outcome. Overall, 30-day mortality is 0.03% (2 cases in professional centers during initial and competent phase) and long-term morbidity is 0.7±0.2% (strictures after esophageal or anorectal ESD) in the 72 ESD centers (6497 ESD; follow-up 41±3 mo).The survey results split into beginners (≤ 30 ESD) and competent to professional category centers (>30 ESD) shows low rates of procedural and oncological sAE of ESD-ITT (Fig. 3): a) surgical repair for ESD AE was needed in 3.5±1.5% vs. 1.7±0.4%; b) surgery was indicated for non-curative ESD in 7.4±1.9% vs. 5.2±0.7%, and, c) local recurrence of cancer was observed in 1.5±0.9% vs. 0.3±0.1%, and progressive disease in 0 vs. 0.4±0.2%. There were no significant differences of sAE rates among both subgroups nor in the comparisons of the 3 subgroups (initial vs. competent vs. professional category).

Discussion

Main goal of this ESD training program in Salzburg was a high number of referral centers that start and implement ESD with low risk in an unsupervised fashion – according to a later-on detailed strategy [2]. To this end, principles and guidelines developed in Japan were conveyed by leading experts from Japan. This primer course program conveyed awareness for the two learning curves: 1) accurate endoscopic staging of early neoplasias for correct ESD indication, 2) know-how and basic training for acquisition of electrosurgical ESD skills, and for 3) the logistic requirements to implement a new ESD center [2]; the reference material was continuously updated (endoscopic atlas; per website: syllabus, lectures, video cases). We registered only highly experienced senior candidates, to reduce the risk of AE, preferred newly recruited referral centers, to minimize repetitive participation or additional candidates from recruited centers. And to foster ESD skills, we strongly recommended continued hands-on training ex-vivo, expert observation, sabbatical at ESD centers in Japan or ESD performance under teaching assistance by a Japanese expert [2, 46]. As collaborators in a joint effort to establish an ESD supply network (Suppl. Information 1), the participants were encouraged to perform unsupervised implementation of ESD based on best case-volume according to prevalence of indications and step-up of technical challenge [2].

What are the merits of the retrospective survey on this program? Categorical feedback information was available for 91% of 135 participating centers (30% zero ESD, 7% published ESD, and 54% with ESD survey data) showing a supply network of 83 ESD centers (61%). The 79 (59%) started or implemented ESD centers had been set up on zero or initial (89.5%) or early competent (10.5%) prior ESD experience (Fig. 1). Hence, this course program was an effective ESD start-up primer for referral centers.

The questionnaire data on unsupervised implementation comprises 91% (72 of 79) of the started or implemented ESD centers. All stated to use ESD indications according to JGES [2], qualified analysis of specimens, and a prospective register for ESD-ITT. The questionnaire only asked for core parameters of the implementation strategy, such as basic performance (organ distribution, en bloc-ESD / hybrid-ESD /PM-EMR)

and sAE relevant for the patients. Hence, these cross-sectional data appear representative for the implementation of ESD centers.

Unsupervised implementation of clinical ESD was prevalence-based, mainly on colorectal lesions (66%→72%) with a step-up approach on colonic (9%→32%, P<0.05) and esophageal neoplasias (6%→15%), and nevertheless with a low risk scenario: low rates of 30-day mortality, long-term morbidity and surgical repair, and satisfactory oncological outcome, such as need for oncosurgery and local recurrence of cancer after ESD-ITT (Fig. 3). Overall, these sAE rates are barely higher than reported from East Asia [47, 48]. - ESGE guidelines reject performance of ESD in the colon during the implementation period, mainly because colonic ESD is more difficult and carries a higher risk of perforation [1, 49, 50]. However, the ESGE curriculum for ESD training did not recognize the safety of prospective European case series of colorectal ESD [42, 43, 45, 50-52]. Most colonic perforations are small and well manageable by endoscopy, whereas rare delayed perforations require surgical repair [43-45, 53-57]. In prevalence-based ESD learning curves, colonic ESD is as safe as rectal and gastric ESD (<1% surgery for overall 8-12% AE) [56, 57](ref 66).

The rate of en-bloc ESD in starting centers (64%) was as low as published for initial learning of colorectal ESD [22, 58](ref 66), but in professional category (88%) nearly reached East Asian standard (>90%) [47, 48]. ESD-ITT included a high rate of hybrid-ESD (26%) on initial vs significantly less on competent (13%) and professional (7.5%) categories. Hybrid ESD is blamed for high rate of AE (as bleeding and perforation) in a meta-analysis that has not distinguished hybrid-ESD performed for technical reasons vs. hybrid-ESD for managing AE of ESD [48]. Our faculty, however, had recommended hybrid ESD for self-completion of difficult ESD-ITT [59]. The high rate of hybrid ESD does not correspond to the low rate of AE, but matches the similar rate of failed self-completion (20-35%) for supervised learning of ESD in Japan [54, 55].

Limitations of this cross-sectional survey are a) *retrospective exploratory design* with potential reporting bias, b) unrevealed additional success factors, and c) missing items such as measured training efficiency, organ-specific ESD subgroup analysis, and curative resection data.

a) The retrospective exploratory design of the survey only shows subsequent successful implementation of ESD centers, but no causal relationship. Course participation (with hands-on training) was priming for the program strategy [2]. Reporting bias is possible in such surveys, but less likely in presence of prospective data registers and match of the survey data with the rates of en-bloc ESD and sAE of Western ESD series [27, 28, 32-34, 43, 48, 52, 56, 60].

b) Caution, the low-risk implementation of ESD centers *depends* on *additional success factors* [2]: conscious selection of the center´s most experienced endoscopist, check list for risk precautions and self-evaluation of performance during unsupervised ESD-ITT (Tabs. 1 in (66) and 4 in [2]).

c) Missing items: The hands-on course was not designed to measure *efficiency* of individual skills training because of the scheduled rotation of the trainees during ongoing ESD procedures (but achieved an average number of 4-5 procedures) [3]. Nevertheless during the first year after the course in 2009, the ESD case load (total, colorectal and esophageal) had more than tripled and the trainees with highest perforation rate did not start clinical ESD [3].

Subgroup analysis only shows a non-significant trend for lower rates of sAE (surgical repair, morbidity; onco-surgery, recurrence of cancer) in competent and professional categories. Organ-specific sAE rates were not significantly different due to small differences and small sample sizes – confirming the overall low risk of sAE during implementation of CR-ESD.

This survey only inquired onco-surgery done for non-curative ESD – as surrogate indicator for correct lesion selection - rather than histologic curative resection (CR). An ESGE curriculum training course program (2013 – 2019) of same hands-on format based on gastric and esophageal hybrid knife-ESD with exclusively European teachers reported more successful implementation of clinical ESD: competence was achieved with 10 ESD followed by professional ESD performance (CR >80%) at 10-20 and 20-30 ESD [61]. That questionnaire was much more detailed, but data is based only on19 participants in spite of more than 250 training slots (i.e. <10% surveyed) [61]. Such rapid progression to competent and professional ESD contrasts

with much longer ESD learning curves worldwide [2, 25-27, 42-45, 48, 53, 54, 56, 57, 60, 62].

Our survey data supports the feasibility and safety of prevalence-based colorectal implementation of ESD, as demonstrated by individual learning curves of mainly course participants [42, 43, 52, 56, 57, 63]. Beyond that, CR is the main indicator for professional status of ESD centers [2]. The CR rates (65-75%) reported from Europe are significantly lower than for professional centers of Japan (80-89%) [22, 26, 28, 32, 41, 47, 60, 62, 64, 65], mainly due to less accurate endoscopic indications including deep submucosa-invasive cancers indicated for surgery, not for ESD [2, 26, 60, 62]. Unfortunately, European guidelines still recommend to evaluate en-bloc ESD specimens with the surrogate standard of "*low risk resection*", "*local risk resection*", and "*high risk resection*" [49, 50], that is standard for evaluation of piecemeal EMR [66], but conceals the merit of en-bloc ESD to the patients: histopathologic CR of early GI cancer [4, 10, 11].

Hence, we recommend to stringently apply JGES criteria to ESD-ITT, including the validated indication criteria for "*ESD with curative intention"*, "*ESD with diagnostic intention*", and "*out of ESD indication*" (i.e. "indication for surgical resection with lymphadenectomy") as well as the histopathologic standard "*curative resection*" [4, 10, 11]. ESGE and National Societies will have to focus guidelines and curriculum courses on professional curative rates (80-90%) for ESD with curative intention.

Conclusions

This survey data supports the feasibility and safety of prevalence-based implementation of ESD procedure mainly in colorectum – provided the endoscopist is experienced in endoscopic indication, electro-surgical technique, and know-how for ESD. This facilitates further implementation and advancement of ESD centers in the West.

Acknowledgements

The organizers of the ten events thank the entire faculty for free tutorial and lessons, the veterinary teams (Dr. F. Schmoll (Vienna, AT), Dr. T. Sattler (Leipzig, DE)) and the endoscopy assistants (Anita Bayer / IVEPA, Vienna) and Song-Sa Dammer (Hildesheim, DE) for technical conduct of the course, and all sponsors (see Supporting Information) for unrestricted educational grants. Special thanks to Dr. Hans-Peter Wild and the Leonie Wild Foundation (Heidelberg-Eppelheim, DE). We acknowledge for single replacement of faculty instructors: Phillip Collet (Giessen, DE), Osamu Goto, Motohiko Kato and Toshio Maehata (Tokyo, JP), Shinichi Baba (Osaka, JP), Manabu Takeuchi (Niigata, JP), Arjun Koch (Rotterdam, NL), Mathieu Pioche (Lyon, FR), Jelle Haringsma (Rotterdam, NL), and Edris Wedi (Göttingen, DE). Highly appreciated is the backing by the Institute of Anatomy of Paracelsus Medical University Salzburg and the endorsement by the European and National Societies: ESGE, ÖGGH, OEGCH, DGVS, DGAV, and IVEPA. Technical support: Jutta Harders, Olympus Europe (Hamburg, DE), Birgit Sandhoefner and Jochen Queck, ERBE Elektromedizin GmbH (Tübingen, DE), Takemasa Kojima and Daniela Schröder, FUJIFILM Europe GmbH (Ratingen, DE).

References

[1] Deprez PH, Bergman JJ, Meisner S, Ponchon T, Repici A, Dinis-Ribeiro M, et al. Current practice with endoscopic submucosal dissection in Europe: position statement from a panel of experts. Endoscopy. 2010;42:853-8.
[2] Oyama T, Yahagi N, Ponchon T, Kiesslich T, Berr F. How to establish endoscopic submucosal dissection in Western countries. World J Gastroenterol. 2015;21:11209-20.
[3] Berr F, Ponchon T, Neureiter D, Kiesslich T, Haringsma J, Kaehler GF, et al. Experimental endoscopic submucosal dissection training in a porcine model: learning experience of skilled Western endoscopists. Dig Endosc. 2011;23:281-9.
[4] Hashiguchi Y, Muro K, Saito Y, Ito Y, Ajioka Y, Hamaguchi T, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. Int J Clin Oncol. 2020;25:1-42.
[5] Ono H. Endoscopic submucosal dissection for early gastric cancer. Chin J Dig Dis. 2005;6:119-21.
[6] Oyama T, Tomori A, Hotta K, Morita S, Kominato K, Tanaka M, et al. Endoscopic submucosal dissection of early esophageal cancer. Clin Gastroenterol Hepatol. 2005;3:S67-70.
[7] Tanaka S, Kashida H, Saito Y, Yahagi N, Yamano H, Saito S, et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc. 2015;27:417-34.
[8] Tanaka S, Oka S, Kaneko I, Hirata M, Mouri R, Kanao H, et al. Endoscopic submucosal dissection for colorectal neoplasia: possibility of standardization. Gastrointest Endosc. 2007;66:100-7.
[9] Yahagi N, Fujishiro M, Imagawa A, Kakushima N, Iguchi M, Omata M. Endoscopic Submucosal Dissection for the Reliable en bloc Resection of Colorectal Mucosal Tumors. Dig Endosc. 2004;16:s89-s92.
[10] Ishihara R, Arima M, Iizuka T, Oyama T, Katada C, Kato M, et al. Endoscopic submucosal dissection/endoscopic mucosal resection guidelines for esophageal cancer. Dig Endosc. 2020;32:452-93.
[11] Ono H, Yao K, Fujishiro M, Oda I, Nimura S, Yahagi N, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. Dig Endosc. 2016;28:3-15.
[12] Wagner A, Zandanell S, Kiesslich T, Neureiter D, Klieser E, Holzinger J, et al. Systematic Review on Optical Diagnosis of Early Gastrointestinal Neoplasia. J Clin Med. 2021;10:2794.
[13] Berr F, Oyama T, Ponchon T, Yahagi N. Atlas of Early Neoplasias of the Gastrointestinal Tract: Endoscopic Diagnosis and Therapeutic Decisions. 2 ed. Cham, SH: Springer International Publishing; 2019.
[14] Muto M, Yao K, Kaise M, Kato M, Uedo N, Yagi K, et al. Magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G). Dig Endosc. 2016;28:379-93.
[15] Oyama T, Inoue H, Arima M, Momma K, Omori T, Ishihara R, et al. Prediction of the invasion depth of superficial squamous cell carcinoma based on microvessel morphology: magnifying endoscopic classification of the Japan Esophageal Society. Esophagus. 2017;14:105-12.
[16] Sano Y, Tanaka S, Kudo SE, Saito S, Matsuda T, Wada Y, et al. Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. Dig Endosc. 2016;28:526-33.
[17] Dinis-Ribeiro M, Hassan C, Meining A, Aabakken L, Fockens P, European Society of Gastrointestinal E. Live endoscopy events (LEEs): European Society of Gastrointestinal Endoscopy Position Statement - Update 2014. Endoscopy. 2015;47:80-6.
[18] Yahagi N, Uraoka T, Ida Y, Hosoe N, Nakamura R, Kitagawa Y, et al. Endoscopic submucosal dissection using the Flex and the Dual knives. Techniques in Gastrointestinal Endoscopy. 2011;13:74-8.

[19] Kahler GF, Sold MS, Post S, Fischer K, Enderle MD. Selective tissue elevation by pressure injection (STEP) facilitates endoscopic mucosal resection (EMR). Surg Technol Int. 2007;16:107-12.
[20] Yahagi N, Neuhaus H, Schumacher B, Neugebauer A, Kaehler GF, Schenk M, et al. Comparison of standard endoscopic submucosal dissection (ESD) versus an optimized ESD technique for the colon: an animal study. Endoscopy. 2009;41:340-5.
[21] Toyonaga T, Inokuchi H, Man-I M, Morita Y, Yoshida M, Kutsumi H, et al. Endoscopic submucosal dissection using water jet short needle knives (Flush knife) for the treatment of gastrointestinal epithelial neoplasms. Acta Endosc. 2007;37:645-55.
[22] Rahmi G, Hotayt B, Chaussade S, Lepilliez V, Giovannini M, Coumaros D, et al. Endoscopic submucosal dissection for superficial rectal tumors: prospective evaluation in France. Endoscopy. 2014;46:670-6.
[23] Farhat S, Chaussade S, Ponchon T, Coumaros D, Charachon A, Barrioz T, et al. Endoscopic submucosal dissection in a European setting. A multi-institutional report of a technique in development. Endoscopy. 2011;43:664-70.
[24] Hochberger J, Wilhelms G, Froelich M, Menke D, Wedi E, Buerrig K-F, et al. Endoscopic Submucosal Dissection (ESD) up to 11 cm for 54 Large Laterally Spreading Tumors or Local Recurrencies in the Recto-Sigmoid. Gastrointest Endosc. 2011;73:AB437.
[25] Hulagu S, Senturk O, Aygun C, Kocaman O, Celebi A, Konduk T, et al. Endoscopic submucosal dissection for premalignant lesions and noninvasive early gastrointestinal cancers. World J Gastroenterol. 2011;17:1701-9.
[26] Probst A, Ebigbo A, Markl B, Schaller T, Anthuber M, Fleischmann C, et al. Endoscopic submucosal dissection for early rectal neoplasia: experience from a European center. Endoscopy. 2017;49:222-32.
[27] Santos-Antunes J, Baldaque-Silva F, Marques M, Lopes J, Carneiro F, Macedo G. Real-life evaluation of the safety, efficacy and therapeutic outcomes of endoscopic submucosal dissection in a Western tertiary centre. United European Gastroenterol J. 2018;6:702-9.
[28] Barret M, Lepilliez V, Coumaros D, Chaussade S, Leblanc S, Ponchon T, et al. The expansion of endoscopic submucosal dissection in France: A prospective nationwide survey. United European Gastroenterol J. 2017;5:45-53.
[29] Dang H, Hardwick JCH, Boonstra JJ. Endoscopic intermuscular dissection with intermuscular tunneling for local resection of rectal cancer with deep submucosal invasion. VideoGIE. 2022;7:273-7.
[30] Dermine S, Leconte M, Leblanc S, Dousset B, Terris B, Berger A, et al. Outcomes of esophagectomy after noncurative endoscopic resection of early esophageal cancer. Therap Adv Gastroenterol. 2019;12:1756284819892556.
[31] Agapov M, Dvoinikova E. Factors predicting clinical outcomes of endoscopic submucosal dissection in the rectum and sigmoid colon during the learning curve. Endosc Int Open. 2014;2:E235-40.
[32] Aslan F, Alper E, Cekic C, Yurtlu DA, Ekinci N, Arabul M, et al. Endoscopic submucosal dissection in gastric lesions: the 100 cases experience from a tertiary reference center in West. Scand J Gastroenterol. 2015;50:368-75.
[33] Bialek A, Pertkiewicz J, Karpinska K, Marlicz W, Bielicki D, Starzynska T. Treatment of large colorectal neoplasms by endoscopic submucosal dissection: a European single-center study. Eur J Gastroenterol Hepatol. 2014;26:607-15.
[34] Chevaux JB, Piessevaux H, Jouret-Mourin A, Yeung R, Danse E, Deprez PH. Clinical outcome in patients treated with endoscopic submucosal dissection for superficial Barrett's neoplasia. Endoscopy. 2015;47:103-12.
[35] Emmanuel A, Gulati S, Burt M, Hayee B, Haji A. Using Endoscopic Submucosal Dissection as a Routine Component of the Standard Treatment Strategy for Large and Complex Colorectal Lesions in a Western Tertiary Referral Unit. Dis Colon Rectum. 2018;61:743-50.
[36] Hobel S, Baumbach R, Dautel P, Oldhafer KJ, Stang A, Feyerabend B, et al. [Single centre experience of endoscopic submucosal dissection (ESD) in premalignant and malignant gastrointestinal neoplasia]. Z Gastroenterol. 2014;52:193-9.

[37] Iacopini F, Saito Y, Bella A, Gotoda T, Rigato P, Elisei W, et al. Colorectal endoscopic submucosal dissection: predictors and neoplasm-related gradients of difficulty. Endosc Int Open. 2017;5:E839-E46.
[38] Omae M, Hagstrom H, Ndegwa N, Vieth M, Wang N, Vujasinovic M, et al. Wide-field endoscopic submucosal dissection for the treatment of Barrett's esophagus neoplasia. Endosc Int Open. 2021;9:E727-E34.
[39] Pimentel-Nunes P, Mourao F, Veloso N, Afonso LP, Jacome M, Moreira-Dias L, et al. Long-term follow-up after endoscopic resection of gastric superficial neoplastic lesions in Portugal. Endoscopy. 2014;46:933-40.
[40] Repici A, Hassan C, Pagano N, Rando G, Romeo F, Spaggiari P, et al. High efficacy of endoscopic submucosal dissection for rectal laterally spreading tumors larger than 3 cm. Gastrointest Endosc. 2013;77:96-101.
[41] Schumacher B, Charton JP, Nordmann T, Vieth M, Enderle M, Neuhaus H. Endoscopic submucosal dissection of early gastric neoplasia with a water jet-assisted knife: a Western, single-center experience. Gastrointest Endosc. 2012;75:1166-74.
[42] Ronnow CF, Uedo N, Toth E, Thorlacius H. Endoscopic submucosal dissection of 301 large colorectal neoplasias: outcome and learning curve from a specialized center in Europe. Endosc Int Open. 2018;6:E1340-E8.
[43] Sauer M, Hildenbrand R, Oyama T, Sido B, Yahagi N, Dumoulin FL. Endoscopic submucosal dissection for flat or sessile colorectal neoplasia > 20 mm: A European single-center series of 182 cases. Endosc Int Open. 2016;4:E895-900.
[44] Spychalski M, Dziki A. Safe and efficient colorectal endoscopic submucosal dissection in European settings: is successful implementation of the procedure possible? Dig Endosc. 2015;27:368-73.
[45] Wagner A, Neureiter D, Kiesslich T, Wolkersdorfer GW, Pleininger T, Mayr C, et al. Single-center implementation of endoscopic submucosal dissection (ESD) in the colorectum: Low recurrence rate after intention-to-treat ESD. Dig Endosc. 2018;30:354-63.
[46] Wagner A, Neureiter D, Ziachehabi A, Kiesslich T, Allgaier HP, Kleber G, et al. Endoscopic submucosal dissection by trainees tutored by Japanese experts: short-term results. Endoscopy. 2018;50:S98.
[47] Daoud DC, Suter N, Durand M, Bouin M, Faulques B, von Renteln D. Comparing outcomes for endoscopic submucosal dissection between Eastern and Western countries: A systematic review and meta-analysis. World J Gastroenterol. 2018;24:2518-36.
[48] Fuccio L, Hassan C, Ponchon T, Mandolesi D, Farioli A, Cucchetti A, et al. Clinical outcomes after endoscopic submucosal dissection for colorectal neoplasia: a systematic review and meta-analysis. Gastrointest Endosc. 2017;86:74-86 e17.
[49] Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015;47:829-54.
[50] Pimentel-Nunes P, Pioche M, Albeniz E, Berr F, Deprez P, Ebigbo A, et al. Curriculum for endoscopic submucosal dissection training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2019;51:980-92.
[51] Mocker L, Hildenbrand R, Oyama T, Sido B, Yahagi N, Dumoulin FL. Implementation of endoscopic submucosal dissection for early upper gastrointestinal tract cancer after primary experience in colorectal endoscopic submucosal dissection. Endosc Int Open. 2019;7:E446-E51.
[52] Spychalski M, Skulimowski A, Dziki A, Saito Y. Colorectal endoscopic submucosal dissection (ESD) in the West - when can satisfactory results be obtained? A single-operator learning curve analysis. Scand J Gastroenterol. 2017;52:1442-52.
[53] Hotta K, Oyama T, Shinohara T, Miyata Y, Takahashi A, Kitamura Y, et al. Learning curve for endoscopic submucosal dissection of large colorectal tumors. Dig Endosc. 2010;22:302-6.
[54] Niimi K, Fujishiro M, Goto O, Kodashima S, Koike K. Safety and efficacy of colorectal endoscopic submucosal dissection by the trainee endoscopists. Dig Endosc. 2012;24 Suppl 1:154-8.

[55] Sakamoto T, Saito Y, Fukunaga S, Nakajima T, Matsuda T. Learning curve associated with colorectal endoscopic submucosal dissection for endoscopists experienced in gastric endoscopic submucosal dissection. Dis Colon Rectum. 2011;54:1307-12.
[56] Steinbruck I, Faiss S, Dumoulin FL, Oyama T, Pohl J, von Hahn T, et al. Learning curve of endoscopic submucosal dissection (ESD) with prevalence-based indication in unsupervised Western settings: a retrospective multicenter analysis. Surg Endosc. 2023;37:2574-86.
[57] Zhang X, Ly EK, Nithyanand S, Modayil RJ, Khodorskiy DO, Neppala S, et al. Learning Curve for Endoscopic Submucosal Dissection With an Untutored, Prevalence-Based Approach in the United States. Clin Gastroenterol Hepatol. 2020;18:580-8 e1.
[58] Iacopini F, Bella A, Costamagna G, Gotoda T, Saito Y, Elisei W, et al. Stepwise training in rectal and colonic endoscopic submucosal dissection with differentiated learning curves. Gastrointest Endosc. 2012;76:1188-96.
[59] Toyonaga T, Man IM, Morita Y, Sanuki T, Yoshida M, Kutsumi H, et al. The new resources of treatment for early stage colorectal tumors: EMR with small incision and simplified endoscopic submucosal dissection. Dig Endosc. 2009;21 Suppl 1:S31-7.
[60] Fleischmann C, Probst A, Ebigbo A, Faiss S, Schumacher B, Allgaier HP, et al. Endoscopic Submucosal Dissection in Europe: Results of 1000 Neoplastic Lesions From the German Endoscopic Submucosal Dissection Registry. Gastroenterology. 2021;161:1168-78.
[61] Kuttner-Magalhaes R, Dinis-Ribeiro M, Marcos-Pinto R, Rolanda C, Koch AD. Endoscopic Submucosal Dissection Skills Transfer to Clinical Practice after Hands-On Workshops: An International Survey. Dig Dis. 2022;40:665-74.
[62] Ronnow CF, Elebro J, Toth E, Thorlacius H. Endoscopic submucosal dissection of malignant non-pedunculated colorectal lesions. Endosc Int Open. 2018;6:E961-E8.
[63] Berr F, Wagner A, Kiesslich T, Friesenbichler P, Neureiter D. Untutored learning curve to establish endoscopic submucosal dissection on competence level. Digestion. 2014;89:184-93.
[64] Ohata K, Kobayashi N, Sakai E, Takeuchi Y, Chino A, Takamaru H, et al. Long-term Outcomes After Endoscopic Submucosal Dissection for Large Colorectal Epithelial Neoplasms: A Prospective, Multicenter, Cohort Trial From Japan. Gastroenterology. 2022;163:1423-34 e2.
[65] Saito Y, Uraoka T, Yamaguchi Y, Hotta K, Sakamoto N, Ikematsu H, et al. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc. 2010;72:1217-25.
[66] Ferlitsch M, Moss A, Hassan C, Bhandari P, Dumonceau JM, Paspatis G, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2017;49:270-97.

Figure legends

Figure 1. Supply network of ESD centers started/implemented by senior workshop participants.
1A. Categories of ESD implementation for the 135 participating centers. Feedback from 73 active centers (29 in initial, 29 in competent and 15 in professional category [*** 1 pre-established ESD center excluded from statistical analysis]) and from 40 centers without implementation (zero ESD). No feedback by 22 centers, 12 with unknown performance status and 10 with ESD publications and assigned performance category (* competent; ** professional) yielding 83 active ESD centers.
1B. Distribution of participating ESD centers (as categorized in Fig 1A) across Europe and the Mediterranean Near East. Circles represent centers, insert color the ESD category: grey = unknown, white = zero, red = initial (≤ 30), green = competent (31 – 150), blue = professional (>150 ESD).
1C. Categorial analysis: **ESD** prior experience of the senior trainee of the 83 active ESD centers – distinguished in 79 started or implemented centers and 4 pre-established *professional* centers at the time of participation. ESD center categories as in Fig. 1A.

Figure 2. Performance of ESD during implementation period.
Organ distribution (A) and technical performance (B) of ESD-ITT (mean±SE) of the 72 responding centers is shown for the center categories inital (red), competent (green), and professional (blue).Total subgroup analyses yields only 5 significant differences as shown, * Hybrid-ESD in 1-3 particles [59].

Figure 3. Adverse outcome during implementation of ESD.
The cross-sectional survey is split into initial category (≤30 ESD (red) ; total 420 ESD; follow-up 18±2.6 mo) vs. competent and professional category (>30 ESD (dark green); total 5676 ESD; follow-up 59±5 mo, initial phase of centers included). There were no significant differences between the two groups nor between the 3 categories in total subgroup analyses. * mortality indicates % per category.

Legends to supporting information

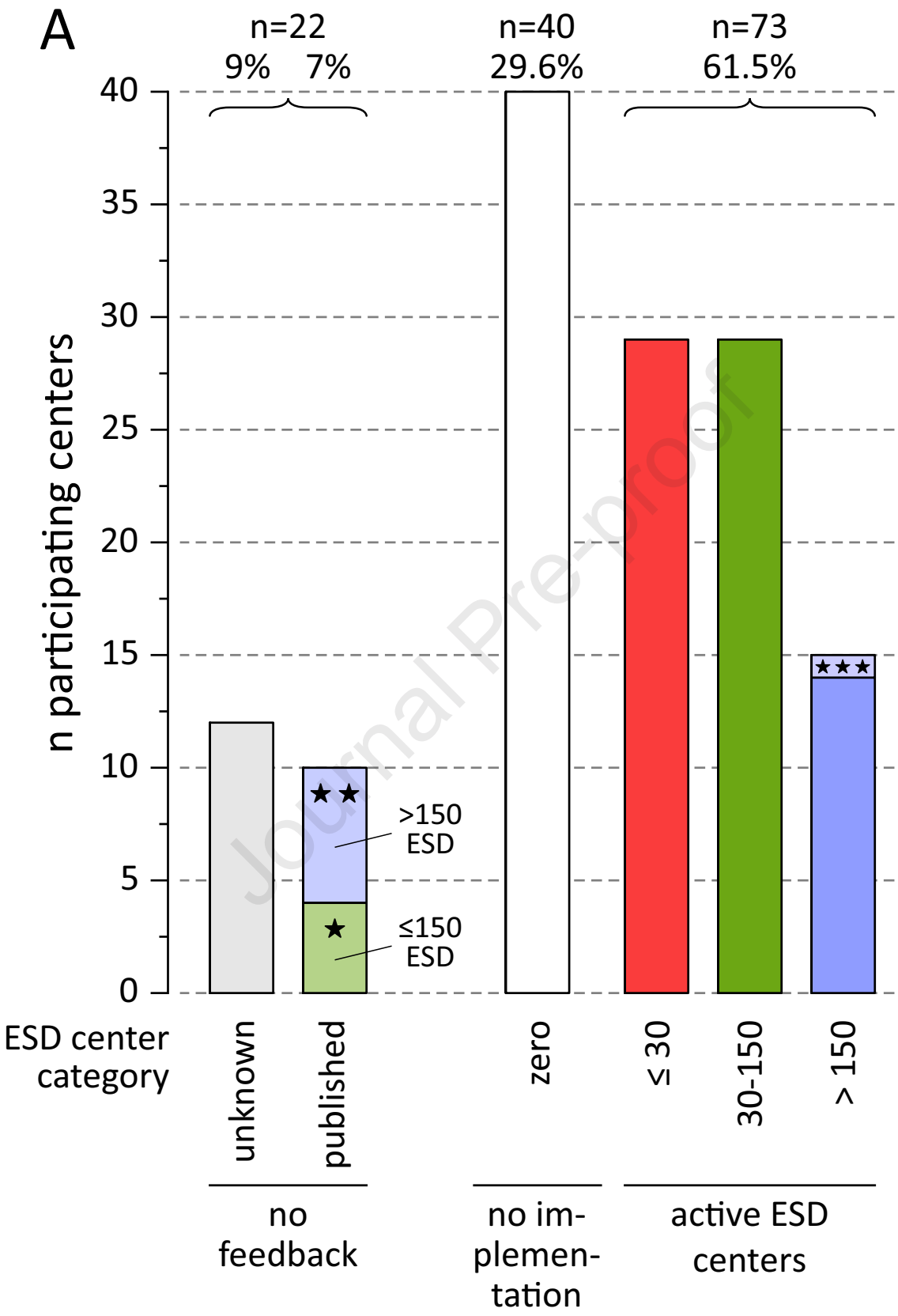
Supporting Information 1. Collaborators - ESD Workshop Training Group (responding centers)

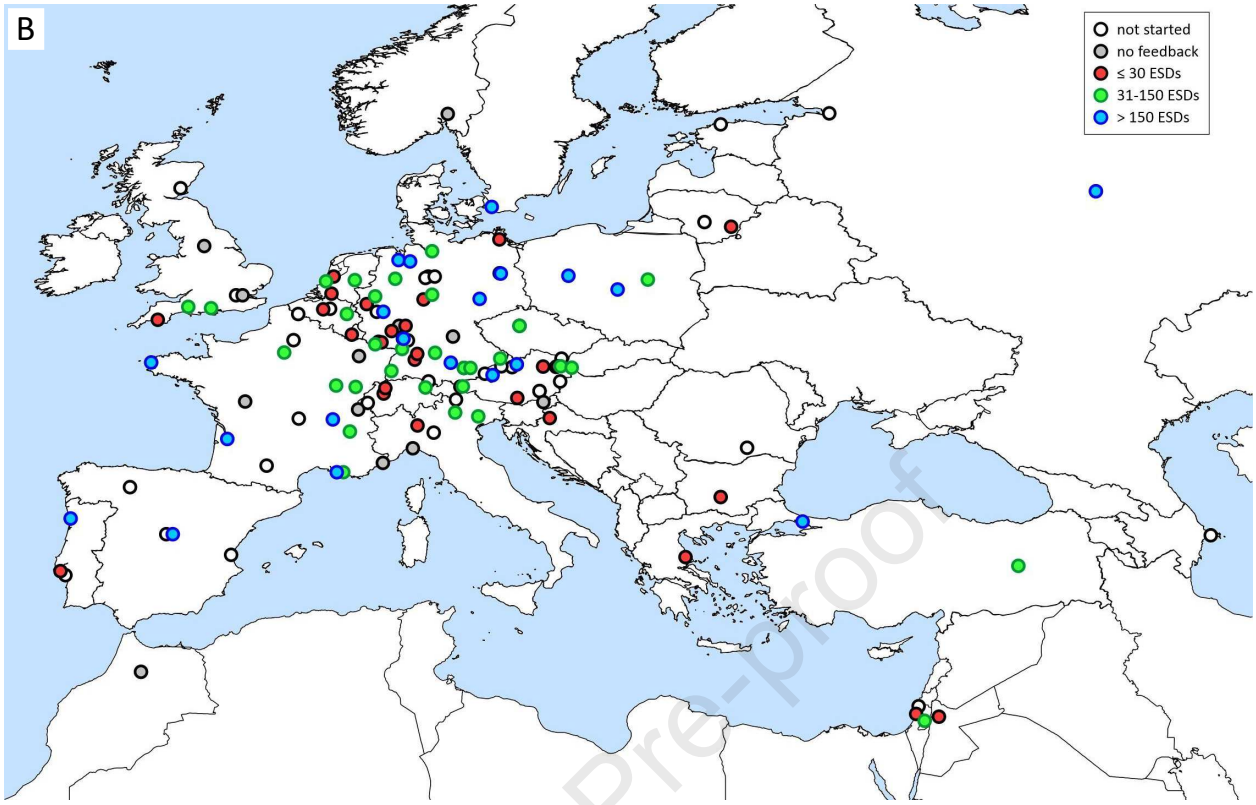
Supporting Information 2. Description of the annual ESD workshop

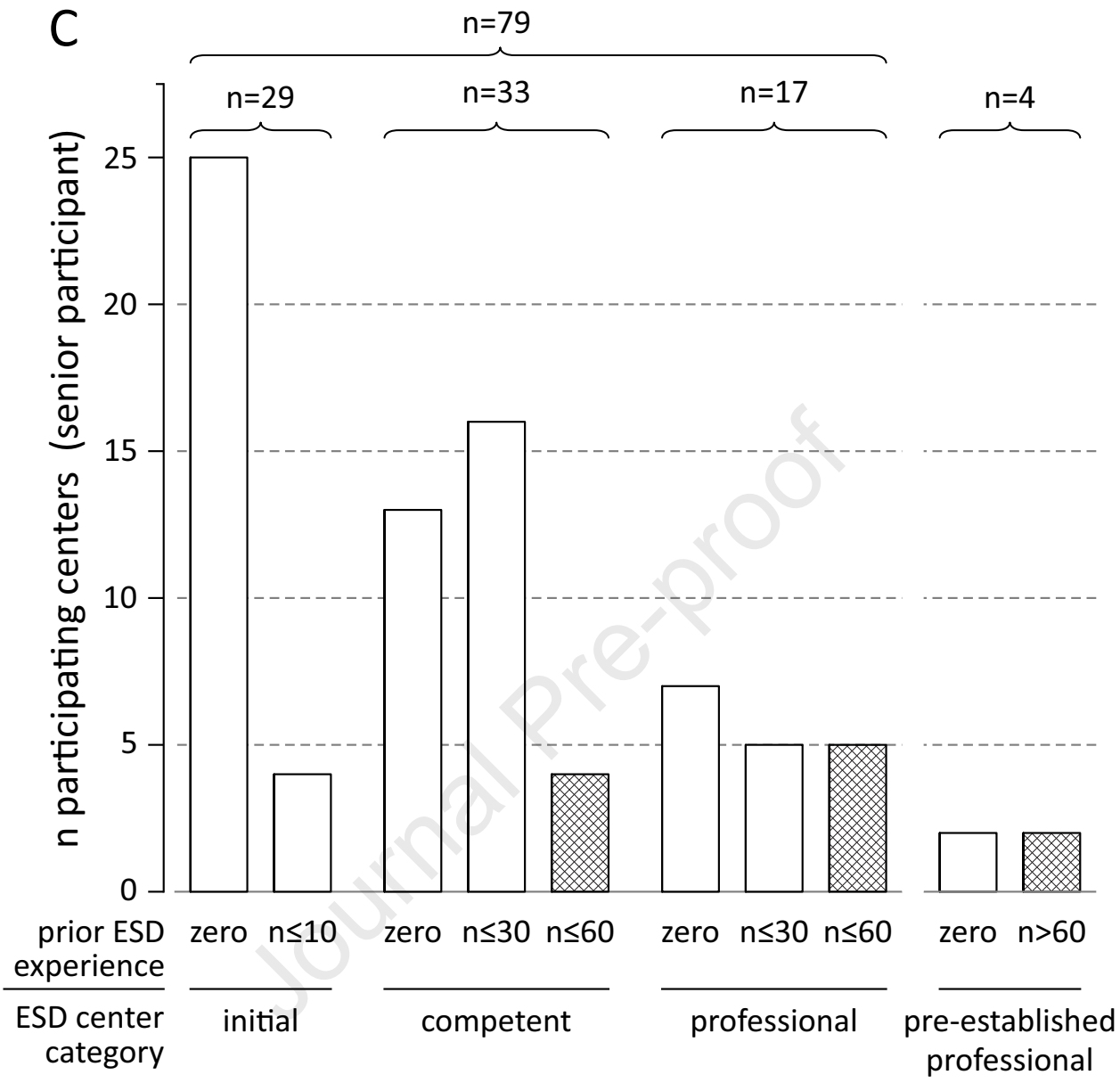
Supporting Information 3. Participants' ESD workshop evaluation 2009-2018

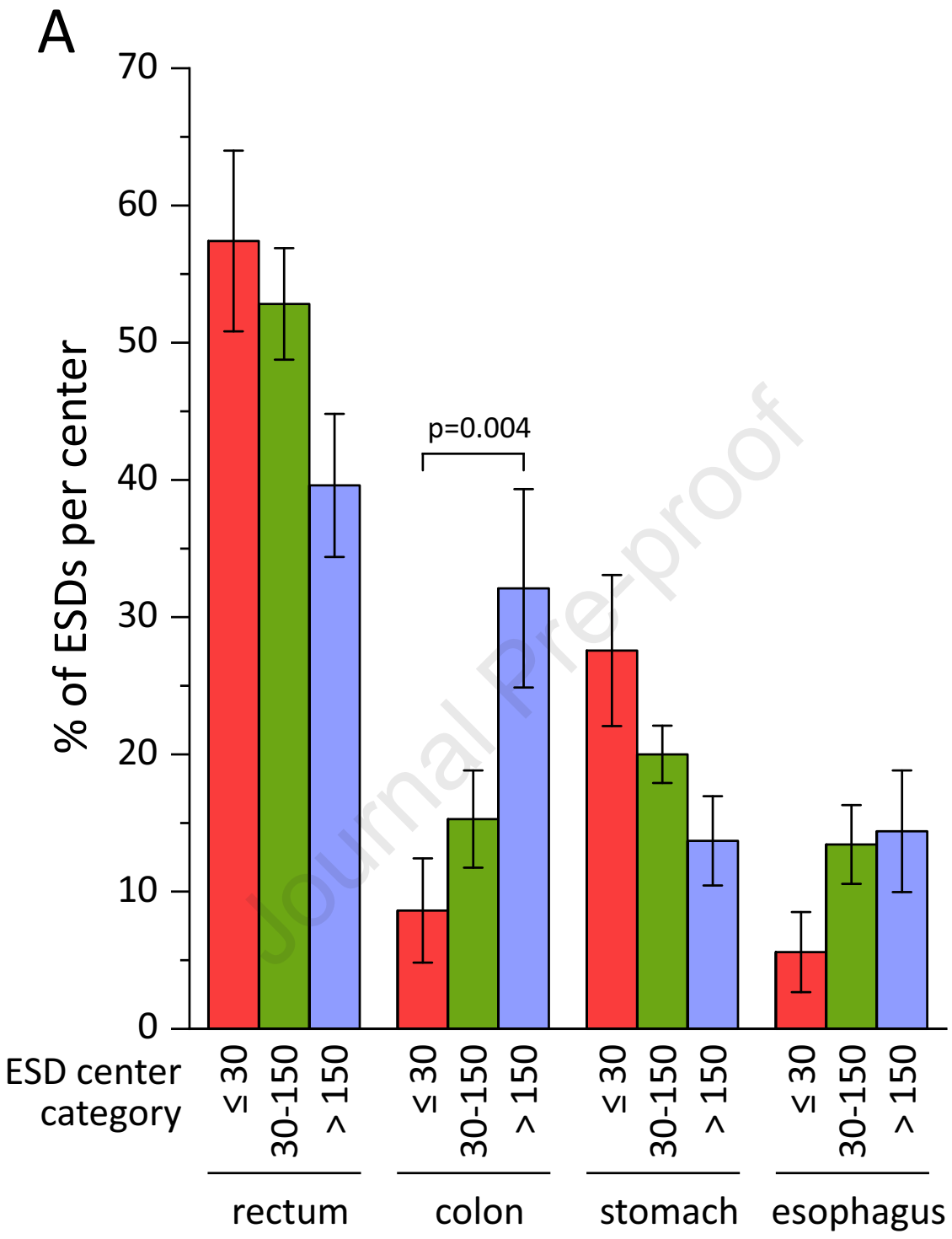
Supporting Information 4. Participants' follow up questionnaire

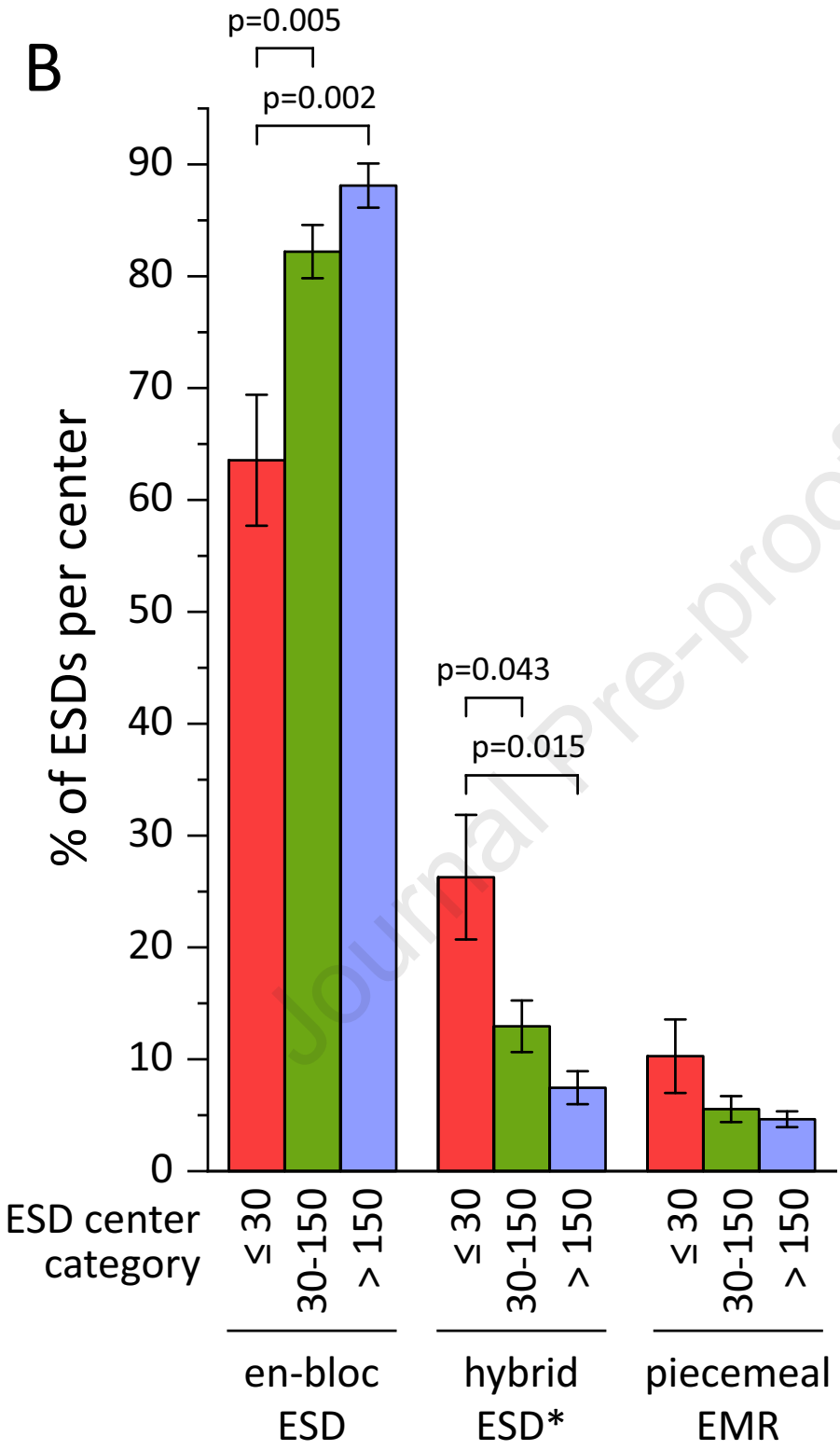
Supporting Information 5. Sponsors of the endoscopic and pharmaceutical industry

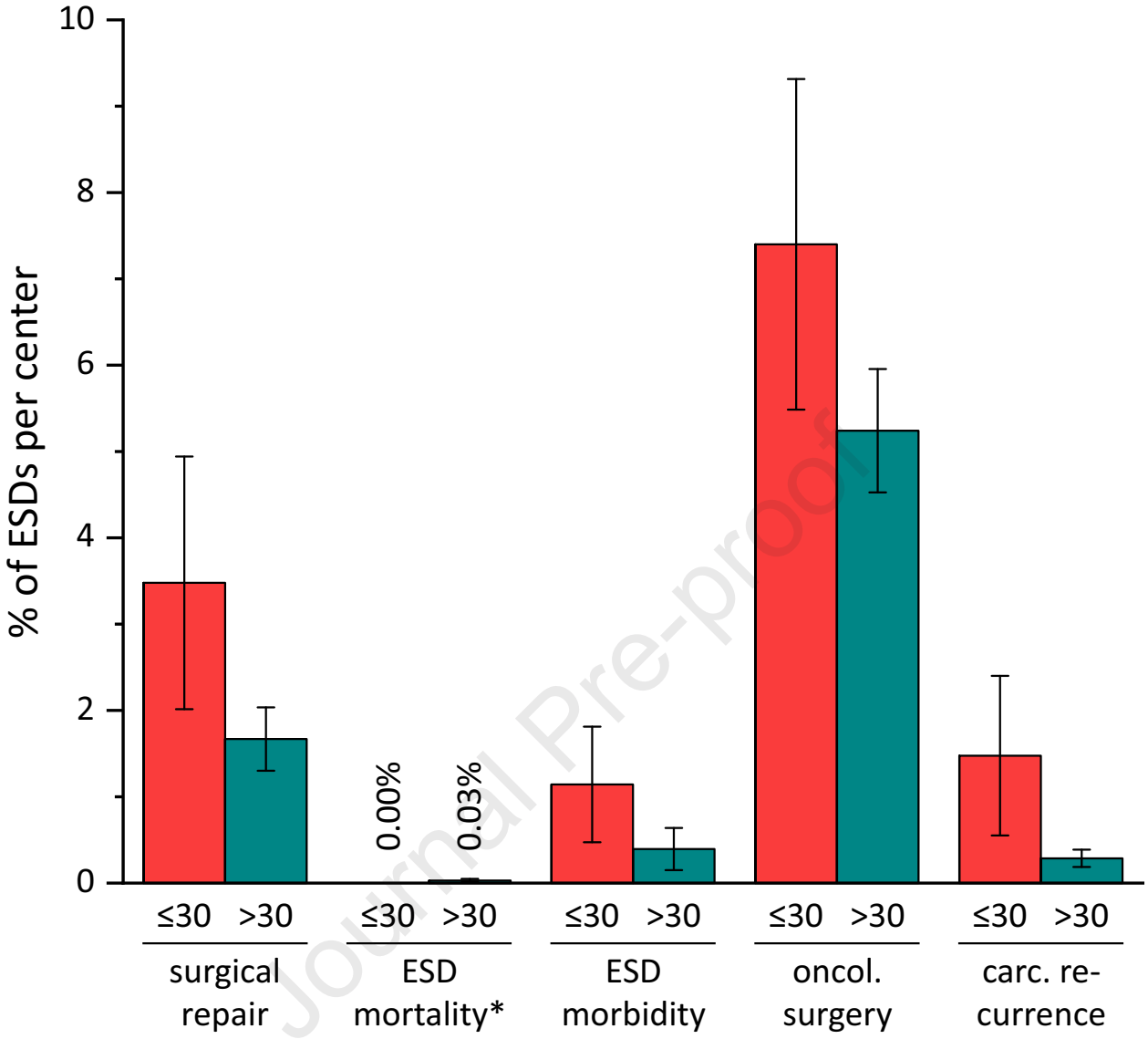












Supporting Information 1

COLLABORATORS - ESD WORKSHOP TRAINING GROUP (responding active centers)

Ulrich Halm, Park-KH Helios, Leipzig, DE
Heinrich Schulz, KH St Josef Bremen, Bremen, DE
Edouard Chabrun, CHU Bordeaux, Bordeaux, FR[1]
Franck Cholet, CHU de la Cavale Blanche, Brest, FR
Henrik Thorlacius, Skane UH, Lund Univ., Malmö, SE
Franz-Ludwig Dumoulin, Gemeinschafts-KH Bonn, DE
Alberto Herreros de Tejada, Porto de Hierros UH, Madrid, ES
Cezary Łozinski, Cancer Institute Poznań, Poznań, PL
Fabrice Caillol, Institut Paoli Calmettes, Marseille, FR
Michal Spychalski, Medical University of Lodz, Lodz, PL
João C Santos-Antunes, Univ Hosp S.João, Porto, PG
Manfred Lutz, Caritasklinikum St Theresia,Saarbrücken,DE
Katrin Bermoser, KH Hall in Tirol, AT[2]
Andreas Schäfer, Alfried-Krupp Krankenhaus, Essen, DE
Yann LeBaleur, CHU Henri Mondor, Paris, FR[3]
Harold Jacob, Haddassah UH, Ein Karem, Jerusalem, IL
Hans-Peter Allgaier, Diakonie KH Freiburg, DE
Gerhard Kleber, Ostalb Klinikum, Aalen DE
Ingo Steinbrück, Asklepios KH Hamburg-Altona, DE[12]
Alberto Tringali, Ospedale Conegliano, Conegliano,IT
Thomas Flatz, LKH Feldkirch, Feldkirch, AT
Christian Österreicher, Hanusch KH, OEGK, Wien, AT
Anton Glas, Klinikum Passau, Passau, DE
Robert Schroder, Gellre Hospital, Apeldoorn, NL[4]
Achim Lutterer, Klinikum Karlsruhe, Karlsruhe, DE
Edri Wedi, Univ Hosp Göttingen, Göttingen, DE
Michael Anzinger, KH Barmherzige Brüder, München, DE
Philip Boger, UH Southampton, Southampton, UK
Stepan Suchánek, Milit. Hosp, Charles Univ, Prague, CZ
Arthur Laquière, Hopital-NORD, Marseille, FR
Sarveson Rajkumar, RoyalStoke UH,Stoke-on-Trent, UK
Maciej Rupinski, Marie Curie OncologyCenter,Warsaw, PL
Terry Jue, Kaiser Permanente Hosp, San Francisco, USA[5]
Mohamed Barawi, UH Wayne State Univ.,Detroit, USA
Christoph Schlag, KH re-dr Isar, Tech.Univ, München, DE
Oliver Möschler, Marienhospital, Osnabrück, DE
Sandro Sferrazza, Univ Hosp. St Chiara, Trento, IT
Boris Pekarek, National Oncology Ctr., Bratislava, SK
Orhan Kursat Poyrazoglu, Firat UH, Elazig, Anatolia, TR[6]
Bulent Baran, Kocaeli Univ. Hosp., Izmit, Kocaeli, TR[13]
Andreas Mayer, Landsteiner UK, LKH, St Pölten,AT
Barbara Tribl, AKH, Wien, Med Univ Wien,Wien, AT
Martin Goetz, Univ.Klinikum, Tübingen, D[7]
Dieter Plamenig, KH Barmherzige Brüder, St Veit, AT[8]
Tilman Pickartz, Univ.Klinikum, Greifswald, DE
Chris Hayward, Plymouth Univ. Hosp. Plymouth, UK
Frank Grünhage, Rhein KH, Dormagen-Grevenbroich, DE[9]
Tarek Qutob, City Hospital, Amman, JD
Tom Seerden, Amphia Hospital, Breda NL
Volker Schmitz, KH Bad Kreuznach, DE
Reiner Wiest, Inselspital, Univ. Bern, Bern CH
Arthur Hoffman, HeliosH-Schmidt KH Wiesbaden, DE
Thomas Flatz, LKH Feldkirch, Feldkirch, AT
Henrik Horvath, Bürgerspital, Solothurn, CH[10]
Edi Viale, Ospedale San Rafaele, Milan, IT
Michaela LaRoche, Diakonie KH Kassel, DE
Jan Peveling-Oberhag, Robert Bosch KH, Stuttgart, DE
Maridi Aerts, ZU Univ Hospital, Brussel, BE
Eyal Gal, Kaplan Medical Ctr, Tel Aviv, IL
Daniel Doykov, Univ Hospital Kaspela, Plovdiv, BGR
David Allerstorfer, KH Rudolfinum, Vienna, AT
Gerd Bodlaj, KH Barmherzige Schwestern, Wien, AT
Romualdas Maskelis, Lithuan. Nat. Cancer Ctr Vilnius, LT
Varvara Vassiljeva, Hospital Arlon, Arlon, BE
Nikos Kapetanakis, Gastro Med Ctr, Volos, GR
Beate Appenrodt, UK Saarland Homburg,DE[11]
Miguel Moura, Santa-Maria-UH, Lisboa, PG
Barbara A Bastiaansen, Acad Med Ctr, Amsterdam, NL
Neven Barsic, Univ Hosp Zagreb, Zagreb, HR
Vinzent Zimmer, Marienhaus Klinik Neunkirchen, DE

Current affiliations:
[1]…*clinique de l'Anjou, Angers, FR*
[2]…*LeopoldinuMED Hall in Tirol, AT*
[3]…*Hôpital Paris Saint-Joseph, Paris, FR*
[4]…*Nij Smellinghe Ziekenhuis, Drachten, NL*
[5]…*Mayo Clinic, Phoenix, AZ, USA*
[6]…*Aydin University Hospital, Istanbul, TR*
[7]…*Med. Klinik IV, Kliniken Böblingen, Böblingen, DE*
[8]…*Spittal a.d. Drau, AT*
[9]… *KRH Klinikum Siloah, Hannover, DE*
[10]…*Klinik Linde, Biel, CH*
[11]…*St. Elisabeth-Krankenhaus, Köln, DE*
[12]…*Diakonie KH Freiburg, DE*
[13]…*Townsville Univ. Hosp. Townsville, Queensland, Australia*

Supporting Information 2. Additional details of the annual ESD course program.

Each annual ESD Workshop has been a priori approved as scientific project by the governmental Ethics Ethics Committee and Animal Ethics Committee (Bundesministerium für Wissenschaft, Forschung und Wirtschaft, Vienna, Austria; BMWF 66.012/0006-II/10b/2009 through 66.019/0029-WF/V/3b/2018), and since 2017 as third party organized procedure training (TPPT) by the Conference Vetting System of Ethical MedTech Europe (www.ethicalmedtech.eu). The ESD Workshops and Updates were operatively organized by the authors located in Salzburg on a not-for-profit basis. Funds for total costs (including accommodation) had been raised from participant fees (40-63%), donations of a charitable foundation (5-25%), and unrestricted educational grants (28-35%) by the endoscopic and pharmaceutical industry.

Description of the annual ESD Training Workshop and Update is given in Methods and for year 2009 in detail [3]. From 2010 on, the attendees were multinational, selected in accordance with ESGE (by T.P.), and ESD-AE were no longer fatal (i.e. no perforation-induced pneumothorax). Since 2010, we focused on training in colorectum, to allow for step-up approach of ESD implementation in colorectum, and improved the structured training program - with 2 parallel training stations per session - for management of bleeding (in heparinized animals), and prevention and management of (intentional) perforation with different techniques (clipping -/+ loop trick; over-the scope clip; endo-suturing). The 4 hands-on sessions (days 1 and 2) were each started with 20 min Live demonstration (knife-type ESD; endo-clipping/-suturing) by a top-expert. In the meantime, stomach or large bowel down from the splenic flexure were cleaned from residual mucus or contents and areas similar to lesions marked with electrocoagulation points by the respective tutor. After a short break to allocate the training teams, the ESD hands-on training run for 4 hours with teams of 3 participants per training station: every 20 min exchange of the operator, every hour move to next working station. Supervision and individualized instruction on the ESD technique was given by the top experts from Japan and experts from Europe and the USA at the parallel stations. ESD specimens were taken to the pathologist to document with image, sizes, ESD type and duration, and AE. In the afternoon session, the teams passed through the corresponding row of training stations. Only very common knife types with cutting direction from near side to far side - hook-(J-)®, dual-(J-)®, hybrid-®, and flush-knife BT® - had been chosen, because learners had been warned of perforation when using knives with cutting direction from far side to near side [8]. In stomach, distal colorectum and – for skilled teams – distal esophagus, different techniques were practiced (as explained in the syllabus): en-bloc ESD using initial circumferential incision (icci), partial circumferential incision (pci), tunneling- and pocket-creating method (pcm), and hybrid ESD (H-ESD with final snaring in 1-3 pieces) [59].

Audiovisual recordings of lectures, quizzes and Live demonstrations of the Update (on day 3) were year-on available on website www.gastroenterologie-salzburg.at, resp. since 2019 for self-learning selected under www.early-cancer.eu. Few of the lectures and the syllabus (last updated in 2020) are available only with password on request from the corresponding author. All updates in course program and supporting material were revised according to JGES recommendations by O.T. and N.Y..

Supporting Information 3. Participants' ESD workshop evaluation 2009-2018

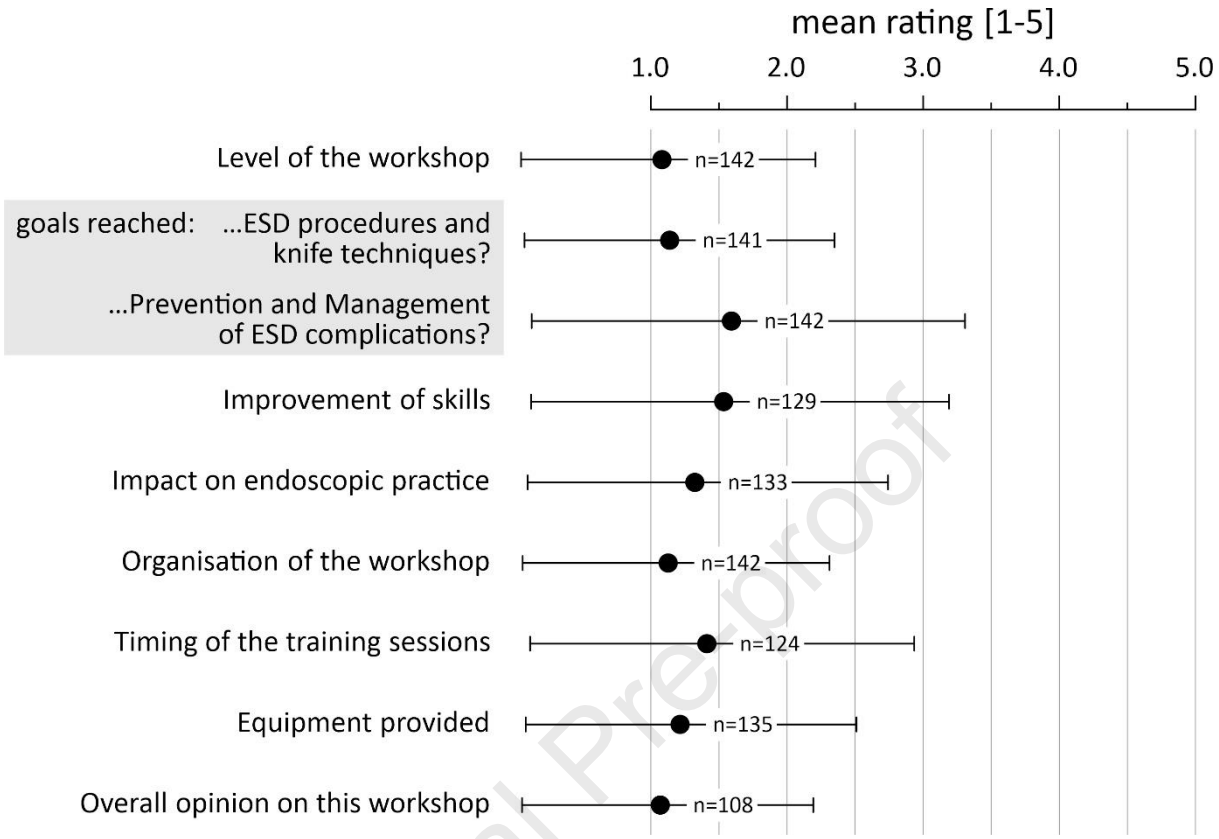


Figure S1. Results of ESD workshop evaluation 2009-2018. Numeric data from a structured questionnaire (see supplementary information 2) which was handed out to all participants in the ESD workshops between 2008 and 2019 are summarized as mean values ± 95% confidence interval. n indicate the number of responses received for each item.

Supporting Information 4. Participants' follow up questionnaire

Basic questions of the Survey Questionnaire "Implementation of ESD technique by participants of ESD Workshops (2009 – 2018)"

"**Feedback 2018** (resp 2019) **after previous ESD WORKSHOP**"

Participation in ESD Workshop *in the year(s)* ……..
Affiliation: ……

Center structure	**YES**	**NO**
• Endoscopic resection …	…	
• Laparoscopic visceral surgery	…	…
• GI pathologist/specimen analysis …	…	
- in serial sections (2 mm)	…	…
- depth of sm invasion (µm) ……		
• ESD indications acc. to JGES*	…	…

ESD performance

Total number of ESD n = … since (month/year): …. / …..

ESD in year 2017: n = …. (resp. in year 2018)

Fraction (%) of all ESD:

- Rectal ESD … %, *malignant* lesions**: …% of *colorectal* ESD
- Colonic ESD … %,
- Gastric ESD … %
- Esophageal ESD … %

Fraction (%) of ESD (*-intention-to-treat)*

- ESD en-bloc … %
- Hybrid-ESD*** … % ***(final snaring, 1 – 3 particles)
- Conversion to piecemeal-EMR … %

ESD with diagnostic intention …%

Severe complications of all ESD (n):

- Surgery for ESD complication n = …
- 30-day mortality n = …
- Long-term morbidity from ESD n = … (impairment: ……)

Follow-up programme after ESD

- Prospective data file (in your center) YES… NO …
- Follow-up recommended (to referring physician) YES… NO …
- Surgery recommended for cure (for non-curative ESD) n = …
- Local / Nodal recurrence of Cancer after ESD n = …
- Progressive Disease after ESD of cancerous lesion n = …

* JGES, Japan Gastrointestinal Endosc. Soc., compare attached Tab 1 [2]
** cancer & HGIEN; *** defined as final snaring in 1-3 pieces [59]

Supporting Information 5. Sponsors of the endoscopic and pharmaceutical industry

SPONSORS OF THE ENDOSCOPIC AND PHARMACEUTICAL INDUSTRY

major sponsors:
Olympus Europe, Hamburg, DE
FUJIFILM Europe GmbH, Ratingen, DE
ERBE Elektromedizin GmbH, Tübingen, DE

3-D Matrix EMEA-BV, Hoofddorp, NL
ALOKA Europe GmbH, Wiener Neudorf, AT
Apollo Endosurgery, Harrogate, UK
Biolitec GmbH, Jena, DE
CliMed GmbH, Vienna, AT
Covidien Austria GmbH, Brunn am Gebirge, AT
Comesa GmbH, Vienna, AT
Cook Osterreich GmbH, Vienna, AT
ENDO Technik W Griesat GmbH, Solingen, DE

Gerhard Pejcl Medizintechnik GmbH, Vienna, AT
Interscope Inc., Worcester, MA, USA
Karl Storz Endoskope SE&Co KG, Tutlingen, DE
Krainer Medizintechnik, Vienna, AT
Leufen Medical GmbH, Aachen, DE
Limbeck Medizin. Spezialartikel, Vienna, AT
A.Menarini Diagnostics GmbH, Vienna, AT
Medi-Globe GmbH, Achenmühle, DE
Medwork Medical Products,Höchstadt/Aisch, DE
MICRO-TECH Europe GmbH
MOSITECH Medizintechnik GmbH, Dornbirn,AT
MTW Endoskopie, 46476 Wesel, DE
OptiMed Med. Instrumente,Wiener Neudorf, AT

Ovesco Endoscopy AG, 72074 Tübingen, DE
Pentax Europe GmbH, Hamburg, DE
Peter Pflugbeil GmbH, Zorneding, DE
PolyDiagnost GmbH, Pfaffenhofen / Ilm, DE
Reinhard Di Lena GmbH, Donnersbach, AT
TOSHIBA Medical Systems, Wiener Neudorf, AT
US Endoscopy Inc., Mentor, Ohio, USA
Werfen Austria GmbH, Vienna, AT

ABBOT GmbH, Vienna, AT
Amgen GmbH, Vienna, AT
Astra Zeneca Austria GmbH, Vienna, AT
Astro-Pharma GmbH, Vienna, AT
Axcan Pharma, 78550 HOUDAN, FR
BAYER Austria GmbH, Vienna, AT
B.Braun Austria GmbH, Maria Enzersdorf, AT
Biolitec Pharma Ltd., Jena, DE
Boston Scientific Austria, Vienna, AT
Chiesi Pharmaceuticals GmbH, Vienna AT
Dako Oesterreich GmbH, Vienna, AT
Dr FALK Pharma GmbH, Freiburg,Breisgau, DE
Emonta Pharma GmbH, Vienna, AT
Fa. EWIMED, 72379 Hechingen, DE
JANSSEN-CILAG Pharma GmbH, Vienna, AT
Limbeck Medizin. Spezialartikel, Vienna, AT
Johnson & Johnson Med. Products, Vienna, AT

Meduna Arzneimittel, 30916 Isernhagen, DE

Merck Austria GmbH, Vienna, AT
Merck Sharp & Dohme Ges.mbH, Vienna, AT
Norgine GmbH, Marburg, DE
Novartis GmbH, Vienna, AT
Nycomed Pharma GmbH, Vienna, AT
Oxford Immunotec Inc, Abington, UK
Pfizer Pharma GmbH, Onkologie, Berlin, DE
ROCHE Austria GmbH, Onkologie, Vienna, AT

Sanova Pharma GmbH, Vienna, AT

Sanofi-Aventis, Österreich, Vienna, AT

Takeda Pharma GmbH, Vienna, AR
Vifor Pharma Österreich GmbH, Vienna, AT
Zymed GmbH, Vienna, AT

Abbreviations

(s)AE	(severe) adverse events
ESD	endoscopic submucosal dissection
ESD-ITT	ESD intention-to-treat
ESGE	European Society of Gastrointestinal Endoscopy
GI	gastrointestinal
H-ESD	hybrid ESD
HGIEN	high-grade intraepithelial neoplasia
IEE	image-enhanced endoscopy
JGES	Japan Gastroenterological Endoscopy Society
LC	learning curve
(PM-)EMR	(piecemeal) endoscopic mucosal resection

Journal CME Conflict of Interest: Disclosure and Attestation

Lead Author: **Frieder BERR** (corresponding author)

Article: **Implementation of Endoscopic Submucosal Dissection in Europe: Survey after ten ESD Expert Training Workshops 2009 – 2018**

Date: **2023-05-31**

PLEASE READ CAREFULLY AND THOROUGHLY.

The American Society for Gastrointestinal Endoscopy (ASGE) is accredited by the Accreditation Council for Continuing Medical Education (ACCME). ASGE must ensure balance, independence, and scientific rigor in all its sponsored educational activities. Anyone in a position to control the content of an activity (i.e., all participating planners, authors, staff, faculty, reviewers, and others in control of educational content) must disclose all financial relationships (of any amount) from the **past 24 months** with any ineligible company directly to ASGE***. ACCME defines an ineligible company as those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.*** Individuals must disclose regardless of their view of the relevance of the relationship to the education.

ASGE Conflict of Interest: ASGE defines a conflict of interest (COI) as involvement in a business, partnership, consulting position, professional society, or a rewarding arrangement that could influence the deliberations or actions of the individual involved with our designated educational activities.

Examples of Ineligible Companies include: Advertising, marketing, or communication firms whose clients are ineligible companies; bio-medical startups that have begun a governmental regulatory approval process; compounding pharmacies that manufacture proprietary compounds; device manufacturers or distributors; diagnostic labs that sell proprietary products; growers, distributors, manufacturers, or sellers of medical foods and dietary supplements; manufacturers of health-related wearable products; pharmaceutical companies or distributors; pharmacy benefit managers; or reagent manufacturers or sellers.

Disclosure information includes: The name of the ineligible company with which you have a financial relationship and the nature of the financial relationship. Examples of financial relationships include employee, ownership interest, researcher, consultant, advisor, speaker, independent contractor (including contracted research), royalties, or patent beneficiary and executive role. Individual stocks and stock options are requested to be disclosed, although diversified mutual funds do not need to be disclosed. Research funding from ineligible companies is requested to be disclosed by the principal or named investigator even if that individual's institution receives the research grant and manages the funds.

Owners or Employees of ineligible companies: Within your disclosure, indicate that you are an owner or employee of an ineligible company. There are ONLY three exceptions that could permit your participation in an ASGE educational activity:

1. When the content of the activity is not related to the business lines or products of your employer/company.
2. When the content of the accredited activity is limited to basic science research, such as pre-clinical research and drug discovery or the methodologies of research, and you do not make care recommendations.
3. When you are participating as a technician to teach the safe and proper use of medical devices and do not recommend whether or when a device is used.

Financial Disclosure

This form must be completed even if you have no financial relationships with an ineligible company. As there is no minimum financial threshold, all individuals must disclose all financial relationships, regardless of the amount, with ineligible companies. Failure or refusal to disclose all financial relationships will result in disqualification from participating in the ASGE CME activity. Following approval, all relevant financial relationships indicated below will be disclosed to all participants/learners in print, electronic, and/or verbally prior to the start of this CME activity.

* We will use email addresses only for questions related to this article

** **Type of relationship may include:** full-time or part-time employee, independent contractor, consultant, research or other grant recipient, paid speaker or teacher, membership on advisory committee or review panels, ownership interest (product royalty/licensing fees, owning stocks, shares, etc.), or any other financial relationship.

The lead author is responsible for submitting the disclosures of all listed authors and must sign this form at the bottom. Additional forms may be submitted if the number of authors exceeds the space provided.

Lead/Primary Author: Frieder BERR **Email Address*: frieder.berr@pmu.ac.at**

X I have no financial relationship(s) to disclose.

Co- Author: Tsuneo OYAMA **Email Address*: oyama@coral.ocn.ne.jp**

X I have no financial relationship(s) to disclose.

Co- Author: Naohisa YAHAGI **Email Address*: yahagi.keio@gmail.com**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Olympus, Fujifilm, Boston Scientific	Consulting fees	
Olympus, Pentax, Boston Scientific	Patents planned, issued or pending	

Co-Author: Thierry PONCHON **Email Address*: thierry.ponchon@wanadoo.fr**

X I have no financial relationship(s) to disclose.

Co-Author: Tobias KIESSLICH **Email Address*: tobias.kiesslich@pmu.ac.at**

X I have no financial relationship(s) to disclose.

Co-Author: Takashi TOYONAGA **Email Address*: toyonaga@bf7.so-net.ne.jp**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Olympus, Fujifilm	Royalties or licenses	

Co-Author: Toshio URAOKA **Email Address*: uraoka@gunma-u.ac.jp**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Olympus Co., Fiji film Medical Co., Boston Scientific Japan	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	

Co-Author: Akiko TAKAHASHI **Email Address*: aurevoireurope@yahoo.co.jp**

X I have no financial relationship(s) to disclose.

Co-Author: Andrej WAGNER **Email Address*: and.wagner@salk.at**

* We will use email addresses only for questions related to this article

** **Type of relationship may include:** full-time or part-time employee, independent contractor, consultant, research or other grant recipient, paid speaker or teacher, membership on advisory committee or review panels, ownership interest (product royalty/licensing fees, owning stocks, shares, etc.), or any other financial relationship.

X I have no financial relationship(s) to disclose.

Co-Author: Alexander ZIACHEHABI **Email Address*:** **alexander.ziachehabi@kepleruniklinikum.at**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
LAMS Lecture and Presentation, Honoraria for HBP Expert meetings, Honoraria for Online Presentation "Treatment of superficial colorectal neoplasia"	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	

Co-Author: Daniel NEUREITER **Email Address*: d.neureiter@salk.at**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Boehringer Ingelheim Pharma GmbH & Co (Germany) and Lilly (Austria)	Consulting fees	

Co-Author: Maria FUSCHLBERGER **Email Address*: maria-fuschlberger@aon.at**

X I have no financial relationship(s) to disclose.

Co-Author: Franz SCHACHINGER **Email Address*: franz.schachinger@gmx.at**

X I have no financial relationship(s) to disclose.

Co-Author: Hans SEIFERT **Email Address*: hansseifert@web.de**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Honoraria from ERBE for tutoring ESD-workshops	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	

Co-Author: Georg KAEHLER **Email Address*: Georg.Kaehler@umm.de**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Micotech Europe GmbH, Baxter, GBUK, Erbe Elektromedizin GmbH, Mediglobe GmbH	Grants or contracts from any entity.	
Dt. Ges. F. Allgemein- und Viszeralchirurgie, EKW-concept GmbH, Köhler Chemie GmbH	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	
Lohmann & Rauscher GmbH, GBUK GmbH	Participation on a Data Safety Monitoring Board or Advisory Board	
Founder and share holder Trans-Duodenal	Leadership or fiduciary role in other board,	

* We will use email addresses only for questions related to this article

** **Type of relationship may include:** full-time or part-time employee, independent contractor, consultant, research or other grant recipient, paid speaker or teacher, membership on advisory committee or review panels, ownership interest (product royalty/licensing fees, owning stocks, shares, etc.), or any other financial relationship.

Concepts GmbH	society, committee or advocacy group, paid or unpaid	

Co-Author: Alexandr MITRAKOV **Email Address*: alexandr_mit@mail.ru**

X I have no financial relationship(s) to disclose.

Co-Author: Sergey V. KANTSEVOY **Email Address*: skan51@hotmail.com**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Olympus, Medtronic, Lumendi, Noah Surgical	Consulting fees	
Lumendi Advisory board	Participation on a Data Safety Monitoring Board or Advisory Board	
Lumendi, Vizballoon, EndoCages, Slater Endoscopy	Stock or stock options	
Endocages (Cofounder)	Other financial or non-financial interests	

Co-Author: Helmut MESSMANN **Email Address*: helmut.messmann@klinikum-augsburg.de**

I disclose the following financial relationships with ineligible companies' commercial entities that produce healthcare-related products or services that could be relevant to this article.

Company	Type of Relationship**	Content Area (if applicable)
Satisfai	Grants or contracts from any entity	
Olympus, Ambu	Consulting fees	
Ambu, Falk, Ispen	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	
Satisfai	Participation on a Data Safety Monitoring Board or Advisory Board	

Co-Author: Juergen HOCHBERGER **Email Address*: juehochber@mac.com**

X I have no financial relationship(s) to disclose.

As corresponding author of this article, I attest that I have received disclosure information from all participating authors as listed above and acknowledge that I am responsible for verifying the accuracy of and reporting completely the information provided to me. Financial relationships relevant to this article can be researched at https://www.cms.gov/openpayments/. I understand that typing my name below serves as an electronic signature for the purposes of this form.

Frieder BERR **Date: 2023-05-31**

Type Name (Electronic Signature)

* We will use email addresses only for questions related to this article

** **Type of relationship may include:** full-time or part-time employee, independent contractor, consultant, research or other grant recipient, paid speaker or teacher, membership on advisory committee or review panels, ownership interest (product royalty/licensing fees, owning stocks, shares, etc.), or any other financial relationship.