U.PORTO

DOUTORAMENTO

CIÊNCIAS MÉDICAS

Training in advanced endoscopic resection techniques

Ricardo Küttner de Magalhães

D

2022

Ricardo Küttner de Magalhães. Training in advanced endoscopic resection techniques

D.ICBAS 2022

U.PORTO

Training in advanced endoscopic resection techniques

Ricardo Sigalho Küttner de Magalhães

INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR

RICARDO SIGALHO KÜTTNER DE MAGALHÃES

TRAINING IN ADVANCED ENDOSCOPIC RESECTION TECHNIQUES

Tese de Candidatura ao grau de Doutor em Ciências Médicas
Programa Doutoral da Universidade do Porto
Instituto de Ciências Biomédicas Abel Salazar

Orientador: **Doutor Arjun D. Koch** (MD, PhD)
Erasmus University Medical Center
Roterdão, Holanda

Co-orientador: **Doutor Mário Dinis-Ribeiro** (MD, PhD)
Professor Catedrático Convidado
Faculdade de Medicina da Universidade do Porto

Co-orientador: **Doutor Ricardo Marcos-Pinto** (MD, PhD)
Professor Auxiliar Convidado
Instituto de Ciências Biomédicas Abel Salazar da
Universidade do Porto
Faculdade de Medicina da Universidade do Porto

“We are what we repeatedly do.
Excellence, therefore, is not an act, but a habit.”

Will Durant

PREAMBLE

Some things could hardly have evolved any better.

The story of this thesis, like that of many other narratives, began without awareness, long before its initial design.

The certainty that my vocation was to be a doctor and that the fulcrum of my activity would always be the sick human being, escorts me since I entered the Faculty of Medicine and has heightened with each passing day.

Interestingly, the perception that medical education was an appealing field and that learning could be different from what I knew, came during my time in the General Surgery internship in Braga. There I was in contact with students who were part of a Medicine course with an innovative approach to teaching. This connection with the surgery territory probably also imprinted traces that would later become visible, when already within the Gastroenterology universe I committed to interventional endoscopy.

During my Gastroenterology residency, I was lucky to get close to Prof. Doutora Carla Rolanda, with whom I have the pleasure to collaborate for years and admire the hands-on courses that, with immense merit and quality, she implemented in Portugal.

Prof. Doutor Mário Dinis-Ribeiro, who deeply influenced a generation of Portuguese gastroenterologists, combining outstanding research with differentiated clinical practice, excels in opening horizons and in his worldwide recognition. So, at the end of my residency period, after introducing me to an advanced endoscopic technique, he mediated an internship at the Erasmus University Medical Center, Rotterdam, under the guidance of Prof. Doutor Arjun Koch.

In the Netherlands, the structure and dynamics of a reference University Department regarding teaching, working, researching and people´s relationships had a huge impact on my development. Prof Doutor Arjun Koch, who seems cut out as no one else to sublimely teach, investigate and work suggested a joint research, where he would lend his knowledge, particularly in his area of interest - endoscopy teaching.

Meanwhile, I started working at the Gastroenterology Department of Hospital Santo António, Centro Hospitalar Universitário do Porto. There, Prof. Doutora Isabel Pedroto, director of the Department and tireless promoter of the clinical progress of its members, along with Prof. Doutor Ricardo Marcos-Pinto, with vast clinical scope, unsurpassed intelligence and dedication to the area of therapeutic endoscopy, embraced the idea.

Together, we agreed to bring the project to Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, with which my Hospital collaborates in medical students training for years.

And so, unparalleled conditions were combined - the area of education, the field of intervention, the possibility of impacting patients, the ideal group of experts involved and the openness of the Institutions of my city.

Even today I can't imagine a greater combination.

May I know how to share with others what I learned throughout this journey.

Index of contents

I. ACKNOWLEDGEMENTS

ACKNOWLEDGEMENTS

The achievement of this thesis was dependent on the collective effort of many people. I would like to pay my recognition, at least to some of them…

To Prof. Doutor Arjun Koch, for the kindness of this opportunity. For having received and taught me in Rotterdam. For his resourcefulness and unique ability to deconstruct complex steps into feasible tasks, whether in teaching differentiated endoscopic techniques or in carrying out research projects. For having opened up a space for me, in which a physician from southern Europe can absorb the best practices from one of the world's leading countries in research and health care. For knowing how to remarkably supervise.

To Prof. Doutor Mário Dinis-Ribeiro, for understanding how to stimulate curiosity in research. For welcoming me into his Department and teaching me endoscopic submucosal dissection during and after my internship. For being available, despite an extremely overbooked schedule. For the mastery in leadership and vision. For the challenges. For the role model.

To Prof. Doutor Ricardo Marcos-Pinto, for having participated and decisively influenced my training, as a resident and continuing to do so today. For the elegance of being a doctor, researcher and endoscopist with outstanding qualities. For wanting to go further. For the motivation and advice. For accepting to mentor this project and allowing to materialize, in the real scenario of our Department, some of the ideas here expressed.

To Prof. Doutora Isabel Pedroto, for molding me early as a resident, for the ability to guide without imposing, to lead by behavior and for opening doors. For the dedication, the perspicacity, the dynamism, the constant encouragement to improve and for the example of dedication to patients, doctors and to our Department.

To Prof. Doutora Carla Rolanda, for having invited me long ago to participate in the simulation courses and for having trusted in me for that task. For her integrity, commitment and for having provoked interest in teaching endoscopy through animal models.

To all the co-authors of the articles, in the persons of Prof. Doutor Marco Bruno, Prof. Doutor Pedro Nunes and Prof. Doutor Diogo Libânio, for their professionalism, rigor and contribution.

To Joana Almeida and Nair Pinto, for the time-consuming task of reviewing the language, the clarity, the grammar and the spelling of this thesis.

To all the members of my Department, to the administrative staff and assistants who supported me in times of fatigue, to the nurses who put up with me for hours, to my medical colleagues who helped and backed me so that this thesis could be built.

To my parents, Ana and Augusto, who were undoubtedly the ones who taught me to be who I am and who have been the foundations of my life. For their unwavering, unconditional support, ranging from the toughest decisions to the most quotidian and practical duties. The example I would like to know how to replicate.

To my children, Inês, Vicente and Constança, for shaping my life, transforming it into dedication and meaning, with endless wonder.

To Ana, for knowing me deeper than I do, for forcing me to evolve, for pointing out the essential things in life, for sacrificing for me, for choosing to be by my side every day, for sharing an inspiring path.

To Ana's family, who is also mine, in the person of Prof. Doutor Filipe Almeida, for being the personification of good. The paradigm of the faultless physician in clinical matters, inspiring and untouchable in all the moral and ethical domains, who always strives to discerns the faire and virtuous route.

To all those who became close - friends, family, doctors, nurses … - and made me better.

II. Outline of the thesis and list of publications

OUTLINE OF THE THESIS

The present thesis is organized according to the following structure.

In Chapter I - ***Acknowledgements*** - a recognition of those who supported the achievement of this project is provided.

In Chapter II - ***Outline of the thesis and list of publications*** - the thesis layout and the scientific publications that permitted its accomplishment are displayed.

In Chapter III - ***Summary*** - a brief description of the thesis is presented.

In Chapter IV - ***Introduction*** - the *rationale* and motivation of the research are explained. Subsequently, the *aims* of the thesis are described. Additionally, *background* information regarding the research topics, such as gastrointestinal neoplasms and strategies for training in advanced endoscopic resection techniques, particularly in endoscopic submucosal dissection (ESD) are addressed.

In Chapter V - ***Simulation in gastrointestinal endoscopy training*** - a review article on simulator training in gastrointestinal endoscopy is presented.

In Chapter VI - ***Animal model simulation for advanced endoscopic resection techniques*** - two aims of the thesis are answered by two original articles exploring the role of the live porcine model. The first establishes the validation of endoscopic mucosal resection/ESD for training and the other evaluates the early learning curve of ESD on this model.

In Chapter VII - ***Endoscopic submucosal dissection training pathways and clinical outcomes*** - two additional aims are addressed through two original articles. One focuses on the acquired training, namely in animal model, by expert endoscopists performing ESD, while the other assesses ESD training pathways of participants of dedicated workshops and its impact on clinical outcomes.

In Chapter VIII - ***Discussion*** - the results of the studies are globally and comprehensively discussed.

In Chapter IX - ***Conclusions and future perspectives*** - the clinical impact of the thesis, major conclusions and potential areas of research are stressed.

LIST OF PUBLICATIONS

The articles that allowed the completion of this thesis are outlined below.

1. **SIMULATOR TRAINING IN GASTROINTESTINAL ENDOSCOPY - FROM BASIC TRAINING TO ADVANCED ENDOSCOPIC PROCEDURES.**

   van der Wiel SE, Küttner-Magalhães R, Rocha Gonçalves CR, Dinis-Ribeiro M, Bruno MJ, Koch AD.

   Best Pract Res Clin Gastroenterol. 2016;30(3):375-387. doi: 10.1016/j.bpg.2016.04.004.

2. **TRAINING IN ENDOSCOPIC MUCOSAL RESECTION AND ENDOSCOPIC SUBMUCOSAL DISSECTION: FACE, CONTENT AND EXPERT VALIDITY OF THE LIVE PORCINE MODEL.**

   Küttner-Magalhães R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD.

   United European Gastroenterol J. 2018;6(4):547-557. doi: 10.1177/2050640617742484.

3. **A STEEP EARLY LEARNING CURVE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN THE LIVE PORCINE MODEL.**

   Küttner-Magalhães R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD.

   Dig Dis. 2021. doi:10.1159/000521429.

4. **ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): HOW DO WESTERN ENDOSCOPISTS VALUE ANIMAL MODELS?**

   Küttner-Magalhães R, Pimentel-Nunes P, Araújo-Martins M, Libânio D, Borges-Canha M, Marcos-Pinto R, Koch AD, Dinis-Ribeiro M.

   Scand J Gastroenterol. 2021;56(4):492-497. doi: 10.1080/00365521.2021.1879251.

5. **ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) SKILLS TRANSFER TO CLINICAL PRACTICE AFTER HANDS-ON WORKSHOPS: AN INTERNATIONAL SURVEY.**

   Küttner-Magalhães R, Dinis-Ribeiro M, Marcos-Pinto R, Rolanda C, Koch AD.

   Dig Dis. 2021. doi: 10.1159/000521274.

III. SUMMARY

SUMMARY

Endoscopic resection procedures are treatment modalities used in clinical practice to manage both pre-malignant and early neoplastic lesions. One of these techniques, endoscopic submucosal dissection (ESD), allows en bloc resection irrespective of lesion size and precise histopathological assessment. It provides higher radical (R0) resection rates and lower local recurrence rates compared to conventional endoscopic mucosal resection (EMR). On the other hand, due to its complexity, ESD involves prolonged procedure times and an increased risk of adverse events. Taking this in consideration, enhanced technical skills are required and, consequently, ESD has a long learning curve. Therefore, endoscopic societies have widely recognized the necessity of adequate strategies to establish comprehensive ESD training curricula. In fact, an endoscopist aiming to start performing ESD should follow step-up training program which involves baseline endoscopic experience, acquiring ESD theory knowledge, observing/assisting procedures, practicing on animal models and, only then, proceeding to clinical practice, under expert supervision. ESD performance on animal models has been recognized as the simulation setting of choice, due to its perceived human similarity. Certainly, general principles of endoscopy training are common in different medical procedures.

The aims of the thesis were: (i) to formally validate the live porcine model in performing EMR, ESD and subsequent complication management; (ii) to evaluate the early learning curve for performing ESD on live porcine model; (iii) to determine how Western endoscopists from referral centers for advanced endoscopic resection techniques have acquired their ESD training and (iv) to assess ESD training pathways of endoscopists participating in dedicated workshops and consequently its clinical impact on ESD outcomes.

To achieve those goals, the realism of the animal model compared to human setting and key ESD procedural performance measures were assessed in hands-on live porcine model EMR and ESD workshops. Additionally, surveys for advanced Western endoscopists performing ESD and for previous participants of live porcine models ESD workshops were conducted.

Face, content and expert validity of the live porcine model in performing multiband EMR, esophageal and gastric ESD was established, by 91 endoscopists participating in 4 workshops. Training in a live porcine model was considered very realistic compared to the human setting, with median global classifications ranging between 7,0-8,0 (IQR 5,0-9,0) on the realism of the model and from 8,5-9,0 (IQR 8,0-10,0) on the execution of the procedures. It was highly appreciated as a learning tool with medians of 9,0-10,0 (IQR 5,0-10,0). In a subsequent study carried out by 17 trainees, performing 70 ESDs,

complete resections, en bloc resections and ESD speed improved (88,2% to 100%; 76,5% to 100%; 8,6 to 31,4mm^2/min, respectively), whereas adverse events decreased (6 to 0), during consecutive procedures.

Furthermore, we realized that Western endoscopists had extensive endoscopic experience before starting ESD and the majority (92%) underwent training with animal models (84% with live animal and 74% with ex vivo). Data concerned 50 endoscopists, from 58 participating experts, that were conducting clinical ESD. Animal models were considered very useful, with ratings of 9,0-10,0 (IQR 8,0-10,0), and deemed a prerequisite before clinical practice by the majority of the endoscopists (84% and 78% for ex vivo and live animal models, respectively). Finally, 40 endoscopists attending ESD workshops with live porcine models, participated in our following research and 19 were performing human ESD. We ascertained that they were adequately skilled prior to clinical ESD practice, with 7,7 years (SD 4,1) of endoscopic experience and all were performing EMR and emergency therapeutic endoscopy. Participants complied with recommendations for training and, in particular, 100% of them trained with live animal models. ESD was properly implemented in clinical practice, with the vast majority starting clinical procedures in the lower third of the stomach or rectum (90%), with lesions with ≤30mm (89%). Overall total en bloc resection rate was 92%, R0 resection rate 88%, curative resection rate 86% and adverse events rate <10%. Only endoscopists who had performed >10 human ESD procedures surpassed predefined clinical competence thresholds.

In conclusion, considering the close resemblance of the animal model to the human setting, its key role as a learning tool, along with the validation of EMR and ESD for training, adequate evidence has been gathered to recommend its incorporation into formal teaching programs. Supporting this assumption, improvement in ESD performance measures was demonstrated by training with such models, which were considered very useful and a prerequisite before clinical practice. Furthermore, endoscopists performing clinical ESD were adequately skilled before human ESD initiation, complying with most of recommendations for training and appropriately implementing the technique in clinical practice. Importantly, we observed that structured training programs translated into clinical outcomes that exceed established standards, namely in the early clinical phase.

RESUMO

Os procedimentos de resseção endoscópica constituem modalidades de tratamento utilizadas na prática clínica para abordar lesões pré-malignas e neoplásicas precoces. Uma dessas técnicas, a disseção endoscópica da submucosa (ESD), permite resseções em bloco, independentemente do tamanho da lesões e avaliação histopatológica precisa. Possibilita portanto, uma taxa de resseção radical (R0) superior e uma taxa de recorrência local inferior, quando comparada com a mucosectomia convencional (EMR). Por outro lado, devido à sua complexidade, a ESD envolve tempos de procedimento prolongados e um risco aumentado de eventos adversos. Desta forma são necessárias competências técnicas avançadas e, consequentemente, a sua curva de aprendizagem é longa. Portanto, as sociedades endoscópicas reconheceram amplamente a necessidade de estratégias adequadas para estabelecer currículos completos de treino em ESD. Efetivamente, um endoscopista com o objetivo de iniciar a técnica de ESD deve seguir um programa de treino gradual que envolve experiência endoscópica de base, aquisição de conhecimento teórico sobre ESD, observação/auxílio em procedimentos, prática em modelos animais e apenas posteriormente, o início da prática clínica, sob supervisão de um perito. A prática da ESD em modelos animais foi reconhecida como o cenário de escolha em simulação, devido à sua presumida semelhança humana. Certamente, os princípios gerais do treino em endoscopia podem ser partilhados por outros procedimento médicos.

Os objetivos da tese são: (i) validar formalmente o modelo porcino vivo na execução de EMR, ESD e a abordagem subsequente de complicações; (ii) avaliar a curva de aprendizagem inicial para a realização de ESD em modelo porcino vivo; (iii) determinar a forma como os endoscopistas Ocidentais de centros de referência para técnicas avançadas de resseção endoscópica adquiriram o treino em ESD e (iv) explorar as estratégias de treino em ESD de endoscopistas que participam em *workshops* dedicados e, consequentemente, o seu impacto clínico nos resultados da execução da ESD.

Para atingir esses propósitos, o realismo do modelo animal relativamente ao contexto humano e as principais medidas de desempenho da execução de ESD foram avaliados em *workshops* práticos de EMR e ESD em modelos porcinos vivos. Posteriormente, desenvolveram-se questionários para endoscopistas avançados Ocidentais que realizavam ESD e para participantes de *workshops* prévios de ESD, em modelos porcinos vivos.

A validação de face, conteúdo e de perito do modelo porcino vivo na realização de EMR *multiband*, ESD esofágica e gástrica foi estabelecida por 91 endoscopistas que

participaram em 4 *workshops*. O treino em modelo porcino vivo foi considerado muito realista relativamente ao contexto humano, com classificações globais medianas a variar entre 7,0-8,0 (IQR 5,0-9,0) no realismo do modelo e de 8,5-9,0 (IQR 8,0-10,0) na execução dos procedimentos. O modelo foi altamente apreciado como ferramenta de aprendizagem, com medianas de 9,0-10,0 (IQR 5,0-10,0). Num estudo subsequente, envolvendo 17 formandos que efetuaram 70 ESDs, as resseções completas, resseções em bloco e a velocidade da ESD melhoraram (88,2% para 100%; 76,5% para 100%; 8,6 para 31,4mm^2/min, respetivamente), enquanto os eventos adversos diminuíram (6 para 0), durante procedimentos consecutivos.

Adicionalmente, constatámos que os endoscopistas Ocidentais detinham ampla experiência endoscópica antes de iniciar a ESD e a maioria (92%) recorreu ao treino com modelos animais (84% com animal vivo e 74% com ex vivo). Os dados reportaram-se a 50 endoscopistas, dentre 58 peritos participantes, que realizavam ESD clínica. Os modelos animais foram considerados muito úteis, com classificações de 9,0-10, (IQR 8,0-10,0) e considerados um pré-requisito antes da prática clínica pela maioria dos endoscopistas (84% e 78% para modelos animais ex e in vivo, respetivamente). Finalmente, 40 endoscopistas que frequentaram *workshops* de ESD com modelos porcinos vivos, participaram na nossa investigação posterior, encontrando-se 19 a realizar ESD em humanos. Verificámos que se encontravam adequadamente qualificados antes da prática clínica da ESD, com 7,7 anos (SD 4,1) de experiência endoscópica e todos realizavam EMR e endoscopia terapêutica de urgência. Cumpriam igualmente as recomendações para o treino e, em particular, 100% obteve treino com modelos animais vivos. A ESD foi devidamente implementada na prática clínica, com a grande maioria a iniciar os procedimentos clínicos no terço inferior do estômago ou reto (90%) em lesões com ≤30mm (89%). Globalmente, a taxa total de resseção em bloco foi de 92%, a taxa de resseção R0 de 88%, a taxa de resseção curativa de 86% e a taxa de eventos adversos <10%. Apenas os endoscopistas que realizaram >10 ESDs em humanos ultrapassaram os limiares de competência clínica predefinidos.

Em conclusão, atendendo à semelhança próxima do modelo animal relativamente ao contexto humano, ao seu papel fundamental como ferramenta de aprendizagem, assim como à sua validação para treino em EMR e ESD, reuniu-se evidência adequada para a recomendação da sua integração em programas formais de ensino. A suportar esta suposição, ficou igualmente demonstrada a melhoria nas medidas de desempenho da ESD através do treino com estes modelos, que foram considerados muito úteis e um pré-requisito antes da prática clínica. Paralelamente, os endoscopistas que executam ESD clínica encontram-se adequadamente qualificados antes do início da ESD em humanos, cumprindo a maioria das recomendações para o treino e implementando

convenientemente a técnica na prática clínica. De salientar a constatação de que os programas estruturados de treino se traduziram em resultados clínicos que ultrapassaram os padrões estabelecidos, nomeadamente na fase clínica inicial.

IV. Introduction

INTRODUCTION

A) RATIONALE

Gastrointestinal (GI) cancers represent a clinical heavy burden worldwide. Esophageal, gastric and colorectal cancers combined represent 19% of total cancers incidence and 23% of cancer related mortality.[1] The 5-year survival for esophageal, gastric and colorectal approaches 11%, 22% and 49%, respectively. For the next decades, a 61% overall increase in incidence and 70% in mortality is estimated, for those malignancies combined.

The majority of GI cancers progress gradually from precancerous neoplastic conditions or lesions to early invasive stages before assuming a disseminated behavior. Within this period, endoscopy allows early detection of cancer or neoplastic precursors, as well as therapeutic interventions. The most common endoscopic resection techniques in this setting are Endoscopic Submucosal Dissection (ESD) and Endoscopic Mucosal Resection (EMR) which have the potential to offer a definite treatment in cases with favorable histological characteristics. In selected patients, when compared to surgery, ESD is associated with a lower rate of adverse events, shorter operative and hospitalization time, lower costs and increase quality of life, with similar oncological outcomes.[2, 3]

ESD was developed in Japan in the mid-1990s and has expanded gradually to other countries, although worldwide implementation has been slow. ESD advantages over conventional EMR are the ability of en bloc, radical (R0) resections of lesions >20mm, lowering the risk of local recurrence and allowing reliable histologic evaluation.[4, 5] However, ESD is a complex, more expensive, time-consuming procedure, requiring high level of expertise and carrying considerable risk of adverse events, such as bleeding and perforation. Accordingly, proficiency can only be reached after extensive training and through a long learning curve.

Common to all complex endoscopic procedures is the fact that excellence in practice should be assured by adequate training. There has been a growing tendence in decreasing the importance of number of procedures in detriment of achieving competence for independent performance.[6] Consequently, efforts have been made to improve the quality of endoscopy training. Nevertheless, the master-apprentice model is still the traditional endoscopic learning method, where teaching is accomplished through human procedures under the supervision of experts. In the particular case of ESD, this is the route generally followed in the East.[7, 8]

However, multiple differences have been recognized as contributors to a different approach to ESD training in the West. The most relevant factors identified are the decreased availability of qualified ESD experts and the lower prevalence of gastric superficial neoplasms. Therefore, direct expert supervision learning and initiation of the technique in the easiest and safest locations, namely in the gastric antrum, is not crosswise feasible, in Western countries.[7, 9-11] Additionally, distinct clinical background and technical experience, as well as a nearly exclusive dedication to ESD has been described for Eastern endoscopists.

As a consequence, structured ESD training programs are recommended.[5, 12-14] These typically include background endoscopic experience, theoretical knowledge, observing/assisting ESD procedures, hands-on training in animal models and starting clinical practice, under the supervision of an expert.

To improve the learning process and achieve initial competence in a safe learning environment, procedure simulation may play an essential role, particularly in the West.[15-17] Animal models, especially live ones, gather more human similarity and are considered the most suited endoscopic simulators for training advanced resection techniques. They offer a realistic tissue sensation, elasticity and haptic feedback, providing breathing movements, heart beats, peristalsis, intraluminal secretions and adequate tissue reaction to injection and electrocautery. It is also possible to deal with bleedings and perforations, although pathological scenarios are usually not able to be reproduced.[12] Costs, availability of dedicated facilities and staff, combined with restricted access to animals and the need to sacrifice them represent the disadvantages of the model.[12, 16, 18-20]

Meanwhile ESD had a widespread dissemination in numerous institutions of Eastern countries but a relatively slow diffusion in the West.[21] Therefore several issues still need to be addressed.

It seems logical to practice advanced endoscopic resections in a live animal model, due to its resemblance with human anatomy and thus hands-on courses with these models are being organized throughout the world.

However, for every technology, method or teaching tool, a scientific basis in the form of a formal validation should first be established before its wide practice application. In particular, ethical justification for animal sacrifice for medical training purposes and justification for financial resources employment are concerns that should have scientific support.

Studies on computer and animal model simulators have demonstrated improvement in endoscopic skills and have proven their validity as educational instruments.[22-28] It was however essential to understand the value of endoscopy simulation training in advanced resection techniques. Formal validation of the live porcine model for performing ESD, EMR and complication management was lacking. Similarly, data on the learning curve for performing ESD on such models were necessary.[22-26]

Recommendations regarding ESD training have been issued, but different institutions have resorted to distinct training strategies. Additionally, it has been suggested that the endoscopic background of Western and Eastern endoscopists might be different but there was no evidence to confirm this. So, it was crucial to gain insight in the real world background and training experience of Western endoscopists already performing the technique.

Despite these training proposals, the widespread implementation of training programs has been heterogenous and direct clinical benefits have not been demonstrated.[29, 30] So, translation into clinical practice of structured training programs, including dedicated workshops and hands-on animal models was needed. Endoscopic simulation appears to be important for some endoscopic procedures, particularly in the early learning curve, avoiding patient involvement in this phase.[22-28] Accordingly, it was necessary to know the role of animal model for ESD training and its adequate position in the training programs. Equally, there were scarce data on how endoscopists implementing ESD were adhering to recommendations for training and how was the technique being introduced in clinical practice.

This research was designed to address the questions previously raised. The aims are presented in the following section.

B) AIMS

The aims of this thesis were the following.

1. To explore the role of simulation in gastrointestinal endoscopy training, incorporating essential techniques and complex procedures.

2. To establish face, content and expert validity of the live porcine model in performing EMR, ESD and subsequent complication management in order to assess its value as a training tool.

3. To evaluate the early learning curve for performing ESD on live porcine models by endoscopists without or with limited previous ESD experience.

4. To determine how Western endoscopists from referral centers for advanced endoscopic resection techniques, performing ESD, have acquired their training, with particular regard to animal models.

5. To assess ESD training pathways of endoscopists participating in dedicated workshops and its clinical impact on ESD outcomes.

C) BACKGROUND

1. GASTROINTESTINAL NEOPLASMS AMENABLE TO ENDOSCOPIC TREATMENT

EPIDEMIOLOGY AND RISK FACTORS

Gastrointestinal (GI) cancers impose a clinical heavy burden worldwide. Esophageal, gastric and colorectal cancers (CRC) combined represent 18,7% of total cancers incidence and 22,6% of cancer related mortality.[1]

Regarding incidence, CRC ranks 3rd, gastric cancer 5th and esophageal cancer 8th, which represent a crude incidence rate of 24,5/100.000, 14,0/100.000 and 7,8/100.000, respectively (figure 1).[31]

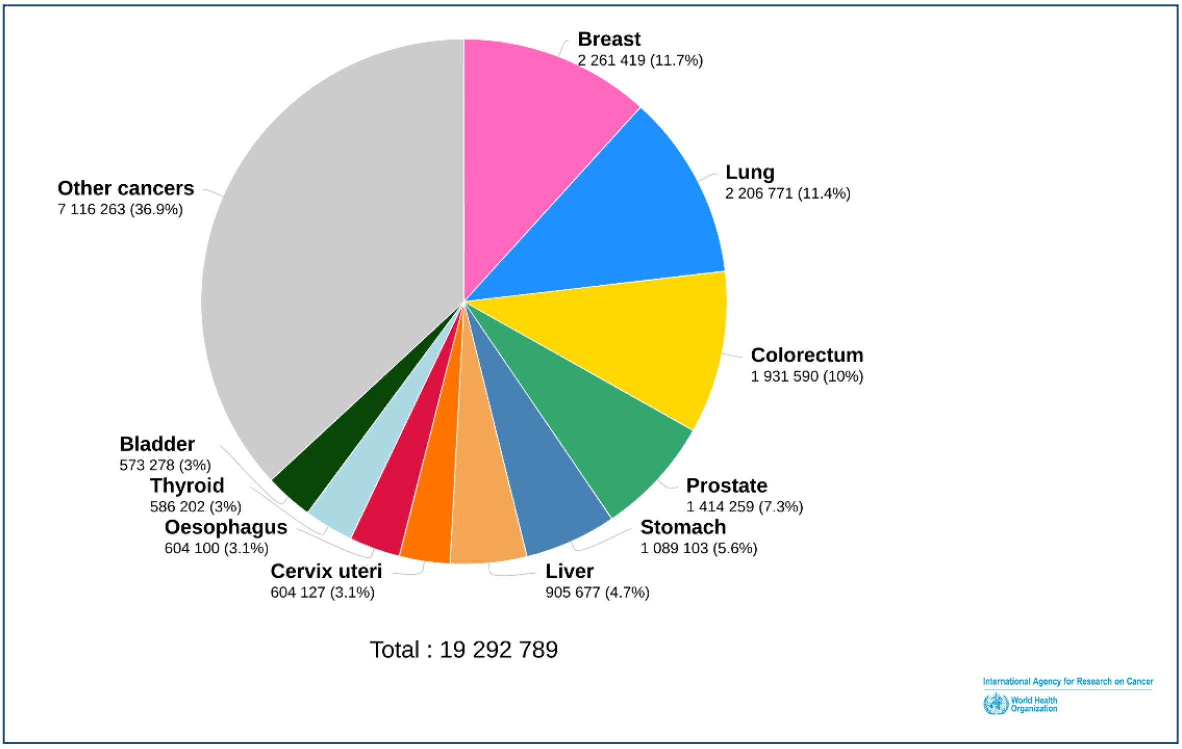

Figure 1. ***Number of new cancer cases in 2020, worldwide, for both sexes and all ages.*** Data from Global Cancer Observatory 2020, International Agency for Research on Cancer, World Health Organization.[31]

Concerning cancer related mortality, CRC ranks 2nd, gastric cancer 4th and esophageal cancer 6th which represent a crude mortality rate of 12,0/100.000, 9,9/100.000 and 6,0/100.000, respectively (figure 2).[31]

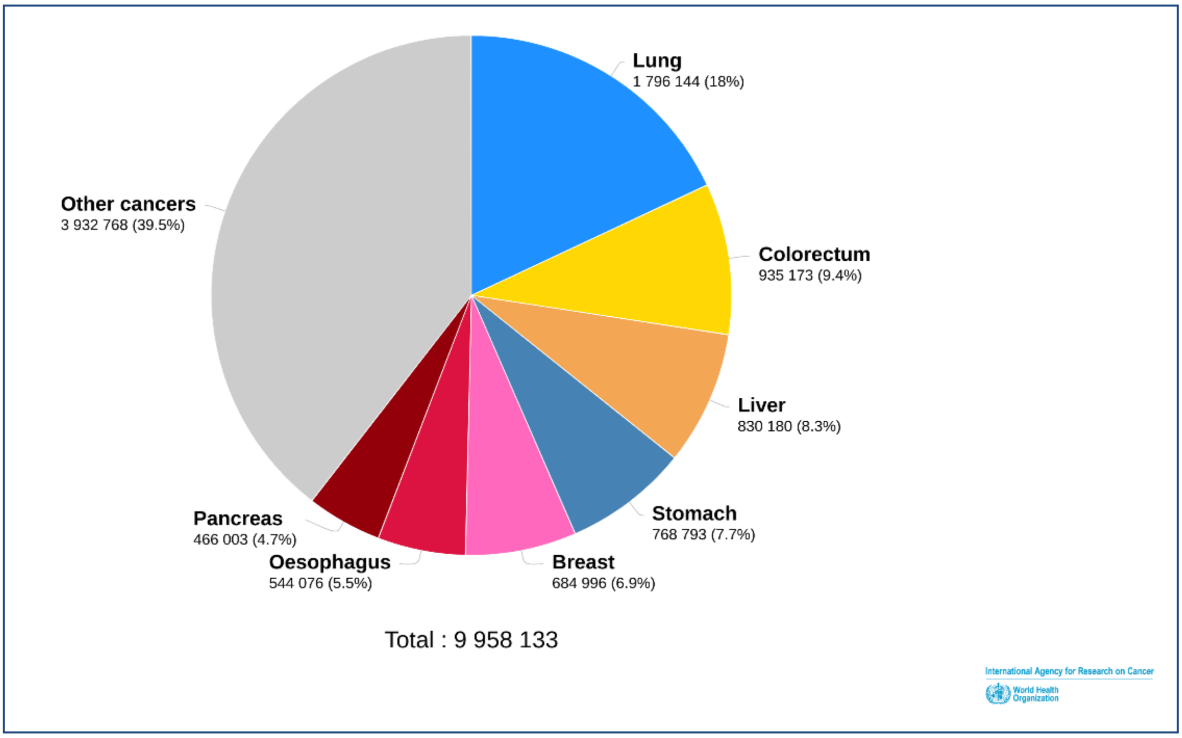

Figure 2. ***Number of cancer deaths in 2020, worldwide for both sexes and all ages.***
Data from Global Cancer Observatory 2020, International Agency for Research on Cancer, World Health Organization.[31]

Usually, GI cancers diagnosed at symptomatic stages involve limited prognosis. The 5-year survival for esophageal, gastric and colorectal cancers approaches 11%, 22% and 49% respectively.[32]

For the next decades, a 60,6% overall increase in incidence and 69,5% in mortality is estimated, for those malignancies combined (figures 3 and 4).[31]

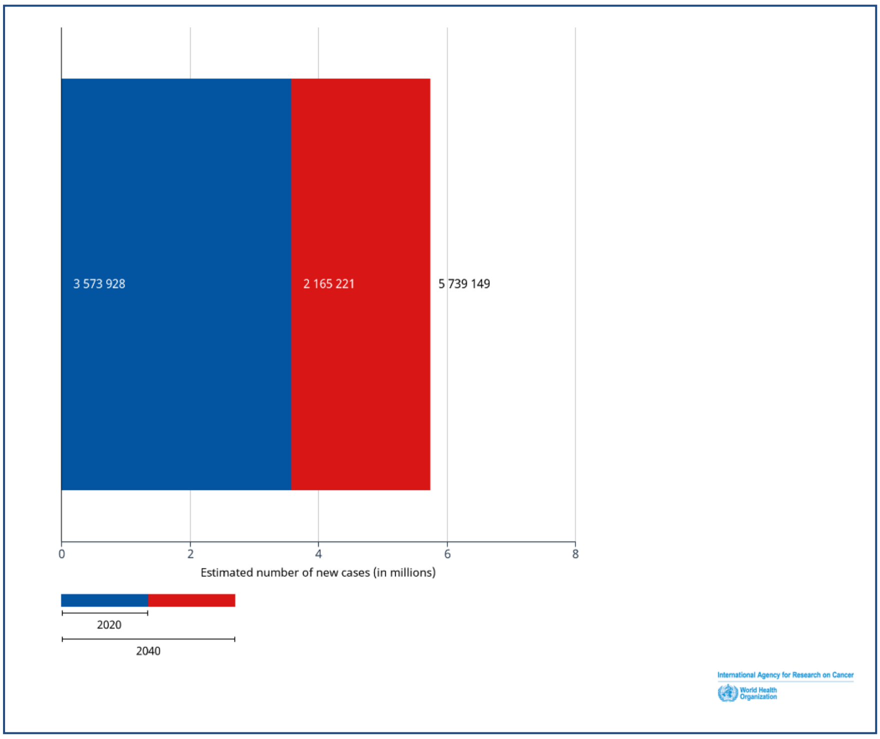

Figure 3. ***Estimated number of new cases of esophageal, gastric and colorectal cancers, from 2020 to 2040, worldwide, for both sexes and all ages.***
Data from Global Cancer Observatory 2020, International Agency for Research on Cancer, World Health Organization.[31]

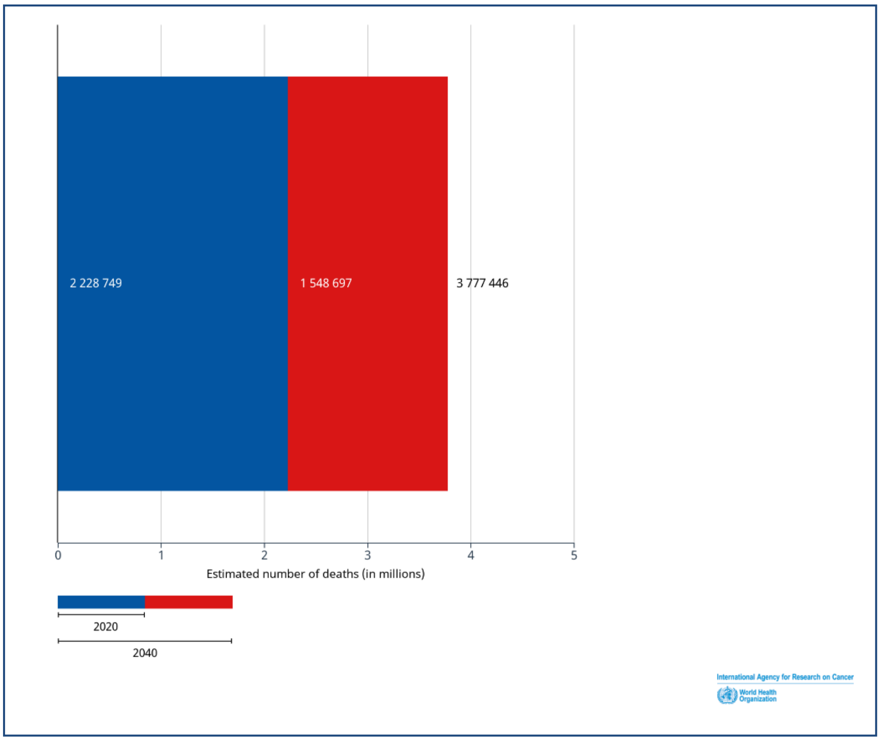

Figure 4. ***Estimated number of deaths for esophageal, gastric and colorectal cancers, from 2020 to 2040, worldwide, for both sexes and all ages.***
Data from Global Cancer Observatory 2020, International Agency for Research on Cancer, World Health Organization.[31]

ESOPHAGUS

The incidence of esophageal cancer has risen in recent decades. The two most common histologic types of esophageal neoplasms are the squamous cell carcinoma (SCC) and the adenocarcinoma. Adenocarcinomas are typically located in the distal esophagus, whereas SCC can develop throughout the whole organ. SCC remain, worldwide, the most prevalent cancer type, particularly in the high-incidence areas of Eastern Asia and in Eastern and Southern Africa.[1, 31, 33, 34] Nonetheless, a marked increase in the incidence of esophageal adenocarcinoma has been observed in Western Europe and North America, matching or exceeding that of esophageal SCC.[35-38]

Esophageal SCC is usually diagnosed at advanced stages when the prognosis is poor.[1, 31, 32] Even in developed countries, the overall 5-year survival rate of patients with esophageal SCC approximates 10%-25%.[32, 38, 39] Smoking and alcohol intake are for the main risk factors.[38, 40] Male gender, black race, previous head and neck cancer and previous esophageal SCC also substantially increase the risk. Achalasia, tylosis, history of caustic ingestion or hot beverages, malnutrition and possibly human papillomavirus infection account for the remaining risk factors.[41-62]

Risk factors associated with the development of esophageal adenocarcinoma are chronic gastroesophageal reflux disease (particularly if increased frequency, severity and duration of symptoms), the presence of Barrett´s esophagus (BE), longer BE extension, increasing age (>60 years), male gender, smoking, obesity, Caucasian race and a family history of BE adenocarcinoma.[35, 63-66] BE is a premalignant condition with an estimated prevalence in the general population of 1% to 2%.[67-73]

STOMACH

Epidemiologic patterns in Western countries are changing, regarding the anatomic location of gastric cancers, with a trend towards decreasing the occurrence of distal or non-cardia gastric cancers.[74-77]

Most gastric cancers in the Western countries are advanced at diagnosis, which is reflected by an overall 5-year survival rate ranging from 20% to 40%. Incidence rates are markedly elevated in Eastern Asia, whereas in Western countries the overall incidence is expected to decrease, although a rise in the total number of cases is estimated, owing to ageing population.[1, 31, 33, 34, 78-81]

Adenocarcinoma accounts for 90% to 95% of all gastric malignancies, comprising intestinal and diffuse types. Acknowledged risk factors for intestinal adenocarcinoma, which is the most common subtype, include *Helicobacter pylori* infection (responsible for up to 75%-89% of all non-cardia gastric adenocarcinomas), conditions such as chronic atrophic gastritis and intestinal metaplasia, smoking, low socioeconomic status, high intake of salty, smoked and preserved foods and low intake of fruits and vegetables. Non-modifiable risk factors comprise advancing age, male gender, family history of gastric cancer, Asian, Hispanic and Blacks races, auto-immune gastritis, gastric adenomatous polyps and Ménétrier disease.[79, 82-85]

SMALL BOWEL

An estimation of 11.390 new cases and 2.100 deaths from small bowel cancer is expected in the United States in 2021.[1, 31, 33, 34] Adenocarcinomas represent the most common type and predominate in the duodenum, followed by lymphomas, sarcomas and neuroendocrine tumors. As a whole, small bowel cancers account for only 4% of all GI malignancies.[86-88]

COLON AND RECTUM

Colorectal cancer is a major cause of morbidity and mortality worldwide. It accounts for approximately 10% of all annually diagnosed cancers worldwide. The pooled 5-year survival in Europe ranges from 46.8% to 49.4%.[1, 31, 33, 34]

Incidence rates are higher in economically developed countries and are either decreasing following a peak, relatively stable or slightly increasing.[89] The decline in CRC incidence and mortality observed in some regions, is presumably related to changing distributions of key risk factors, early detection of cancer and removal of precancerous polyps through screening, in addition to advances in surgical and other treatment modalities.[90-93]

Approximately 70–90% of CRCs develop from the traditional adenoma–carcinoma pathway (chromosomal instability sequence), 10–20% from the serrated pathway, 2%-7% from the microsatellite instability pathway and <2% from the inflammatory pathway.[94, 95] The most common histologic type of CRC is the adenocarcinoma.[94, 95]

Male sex, increasing age (70% of patients are diagnosed after the age of 65 years old) and race/ethnicity (African Americans) are associated with increased disease incidence.[96-99] Of note, an increase in incidence rate has been recorded in the 20 to 49 years-old age group.[100-102]

A positive family history is present in approximately 10 to 25% of cases.[103-107] A subgroup, accounting for <7% of CRCs, is affected by a well-defined hereditary CRC syndrome, such as Lynch syndrome or Familial Adenomatous Polyposis.[108-111]

Patients with long-standing inflammatory bowel disease (especially after 8 years) and those with a previous personal history of CRC or adenomas are at an increased risk for CRC and require adequate surveillance.[112-119]

Smoking, increased bodyweight, excessive alcohol, red and processed meat intake represent the modifiable risk factors.[89, 90, 120-123] Imbalance in gut microbiota might also increase the risk for CRC.[124-126]

EARLY DIAGNOSIS

It has been recognized that the majority of GI cancers gradually develop from precancerous neoplastic conditions or lesions to early neoplastic stages, before assuming an invasive behavior. Endoscopy allows early detection of cancer or neoplastic precursors and potential therapeutic interventions, within this period.[127]

Screening describes the process of early detection or prevention of cancer in average-risk, asymptomatic populations. Surveillance involves the regular follow-up and testing of individuals with a presumed increased risk of cancer following a diagnosis or resection.

The benefit of cancer screening is related to the ability to detect malignancies at pre symptomatic stages, allowing early treatment, thereby, reducing cancer mortality. When treatment for earlier-stage cancers is associated with fewer side effects than the treatment for advanced ones, cancer morbidity may also be reduced. In addition, for some cancer types and screening modalities, prevention of the occurrence of cancer by identifying and removing its precursor is possible, consequently diminishing cancer incidence.[127-129]

On the other hand, potential harms of screening include the possibility of serious test-related complications, such as colonoscopy related perforations, false-positive tests (inducing anxiety and leading to additional invasive diagnostic procedures), overdiagnosis (when cancer detection would not become clinically apparent in the absence of screening) and also overtreatments.[128-131] Similarly, regarding surveillance, inappropriate over and under use has been reported.[132-136]

The “ideal” screening test should be non-invasive, inexpensive, readily available, convenient, safe and ought to possess a high sensitivity and specificity.[128-131, 137]

There are several non-invasive methods for GI cancers, including cytology based (swallowed brush, deflated balloon, sponge), blood markers, breath markers, fecal markers, imaging tests, etc.[138-150]

Endoscopic modalities involve conventional endoscopy (white light and chromoendoscopy), ultrathin transnasal endoscopy, endocytoscopy, microendoscopy and video capsule endoscopy.[151-160]

Endoscopy has been considered the procedure of choice for the diagnosis and when appropriate, treatment of GI neoplastic lesions. It is relatively available, accurate and minor invasive. Therefore, the existence of endoscopically detectable and treatable

GI cancer precursors/early cancers, as well as recurrent lesions, endows endoscopy a critical role.

ESOPHAGUS

Worldwide unselective screening for esophageal cancer would result in a minimal decrease in mortality and in potential serious adverse events, if an endoscopy based strategy would be employed.[128, 129, 161, 162] Since the majority of esophageal cancers are detected at advanced stages, screening high-risk individuals might be beneficial, by allowing cancer detection at earlier stages, which will probably translate into better outcomes.

In the particular case of BE, the risk of cancer progression for patients with a non-dysplastic epithelium is approximately 0.12–0.5% per year.[163, 164] Esophageal cancer in BE evolves from chronic esophagitis, non-dysplastic metaplasia, low-grade dysplasia (LGD), high-grade dysplasia (HGD) and ultimately leading to adenocarcinoma. For patients with LGD or HGD, the annual risk of progression to cancer is approximately 0.7% and 7% per year, respectively.[68, 165, 166]

Screening for BE can potentially prevent esophageal adenocarcinoma and should be considered in high risk populations, such as patients with long standing gastroesophageal reflux disease symptoms (>5 years) and various risk factors, namely age ≥ 50 years, male sex, white race, obesity and a first-degree relative with BE or adenocarcinoma.[64, 68, 165]

Surveillance guidelines for patients with the diagnosis of BE recommend endoscopy from 2/3 to 5 years interval, stratifying patients according to the length of the Barrett's segment, until the age of 75 years-old (extension up to 80 years-old can be considered on an individual base).[165, 166]

It is however important to notice that most cancers are diagnosed at the time or within a year of the index endoscopy and not during latter surveillance.[64, 163]

Despite this agreement on screening and surveillance, the majority of patients diagnosed with BE will die of causes unrelated to esophageal adenocarcinoma.[64]

Regarding SCC, its development occurs through a dysplasia pathway, in which premalignant lesions progress from low-grade intraepithelial neoplasia to high-grade intraepithelial neoplasia, culminating in invasive cancer.[38, 167]

Early detection of SCC, whether cytologic or endoscopy based, has been attempted. In countries with a high incidence of such malignancy, reductions in the incidence and cumulative mortality associated with screening have been demonstrated and may be cost-efective.[168-170]

In moderate and low risk Western countries, the incidence of SCC is relatively low and screening may be considered for individuals perceived to be at higher risk. These high-risk groups include patients submitted to curative treatments for head and neck cancer, with previous caustic injury, tylosis or achalasia. Surveillance should be offered to patients with previous endoscopic resection of SCC.[156, 171, 172]

STOMACH

Screening enables detection of gastric cancer precursors and early gastric cancers, amenable to curative endoscopic treatment modalities. Screening programs have been established in high incidence regions, namely in Japan, South Korea and China, where a 40% reduction in cancer related mortality has been reported.[173-176] Interestingly, in some European countries, early gastric cancer diagnosis has also recently been increasing and survival rates improving.[80]

Intestinal type adenocarcinoma represents more than 95% of gastric adenocarcinomas and is the predominant form in areas of high incidence of gastric cancer. It is accepted as the last step of a lengthy process in which the gastric mucosa evolves to chronic gastritis, then to preneoplastic conditions, such as multifocal atrophy and intestinal metaplasia, subsequently to dysplasia and finally into invasive carcinoma. The process is influenced by host factors, *Helicobacter pylori* infection and particular genotype, as well as environmental exposures, such as dietary salt intake, nitrates and tobacco.[177-179]

In high-risk areas (with an age-standardized incidence rate ≥ 20 per 100 000), endoscopy has a clear role for primary screening and should be considered for individuals aged more than 40 years.[127, 176]

In the general Western population, with an age-standardized incidence rate of <10 per 100 000, screening is not cost-effective and not recommended.[127, 175, 180] However it may be advised for specific subgroups in Western countries, particularly for individuals of Asian origin.[181]

For intermediate-risk regions, with an age-standardized incidence rate between 10 and 20 per 100 000, endoscopy may have a role as a primary screening tool, based on local settings, availability of endoscopic resources and assurance of cost–effectiveness.[127, 182] This strategy may be cost effective, even in Western countries.[181, 182]

Screening for the diffuse type of gastric cancer is not indicated.[127]

The usually slow progression of the intestinal type adenocarcinoma carcinogenesis pathway allows surveillance of patients with premalignant conditions, in selected settings and endoscopic treatment of premalignant or early neoplastic lesions.

Atrophy and particularly intestinal metaplasia may significantly increase the risk of gastric cancer. In patients with chronic atrophic gastritis, the annual incidence of gastric cancer approaches 0.1% to 0.25%, whereas the cumulative incidence ranges between 1.9% and 10% at 5 years to 2% at 20 years.[183] In patients with intestinal metaplasia, the annual incidence of gastric cancer approaches 0.25% whereas cumulative incidences range between 5.3% to 9.8% at 5 years, to 2.4% at 10 years and 2.5% at 20 years.[184-190]

Endoscopic surveillance proposals take into consideration the presence and extension of atrophic changes or intestinal metaplasia, completeness of intestinal metaplasia, existence of family history of gastric cancer, autoimmune gastritis and persistence of *Helicobacter pylori* gastritis. Scheduled intervals vary between 1 to 5 years.[186, 191] Surveillance is recommended for patients with previously resected preneoplastic or early neoplastic lesions. It should also be considered in patients with previous partial gastrectomy and hereditary gastric cancer syndromes, namely Hereditary diffuse gastric cancer, Peutz-Jeghers syndrome, Lynch syndrome, Hereditary breast and ovarian cancer syndrome, Li-Fraumeni syndrome and Juvenile polyposis.[5, 127, 191]

COLON AND RECTUM

Taking into consideration the prevalence of CRC, the general slow growth of primary lesions, the ability to identify higher risk groups, the increased survival of patients with early-stage lesions, the relative access and accuracy of screening tests, CCR screening is essential.

A feature of the majority of CRC carcinogenesis is the presence of a premalignant precursor lesion, that gradually progresses through the acquisition of genetic and epigenetic abnormalities. Identifying and resecting such lesions interruptus this sequence.[192-197]

Screening reduces CRC incidence and/or related mortality by preventing the development of CRC through removal of these precancerous lesions and by early diagnosis.[192-197]

Colonoscopy represents the gold standard for diagnosis of colorectal cancerous and precancerous lesions, with a high sensitivity and specificity. It is also ideal for the detection of sessile serrated lesions.[148, 194, 196] However, it requires bowel preparation, implies considerable costs and is associated with potential adverse events, such as bleeding or perforation in approximately 0.1% to 0.2% of patients.[198, 199] Screening has been demonstrated to be cost-saving or cost-neutral.[200, 201]

For the average-risk Individuals, most countries recommend screening between ages 50 and 75 years-old. American recommendations suggest starting at the age of 45, due to a trend for increasing risk of CRC in adults younger than 50 years and also consider extending it to 85 years taking into account the overall patient's health status (life expectancy, comorbid conditions), prior screening history, as well as individual preferences. In individuals with family history of CRC or advanced polyps, initiation of screening at the age of 40 year-old or 10 years before the youngest affected relative has also been suggested.[127, 137, 197, 199, 202-206]

Surveillance is manly recommended for patients after polypectomy/endoscopic mucosal resection, according to family history, number, size and histology of polyps, as well as completeness and polypectomy technique (en bloc vs piecemeal).[207, 208] Patients after CRC resection or with hereditary GI syndromes (such as Lynch syndrome, Familial Adenomatous Polyposis, MUTYH-associated polyposis, Peutz-Jeghers syndrome, Serrated polyposis syndrome) must also be under surveillance.[108, 209] The same is true for patients with inflammatory bowel disease colitis, in which surveillance intervals varies according to the extent, severity and duration of inflammation, previous history of dysplasia, strictures, inflammatory polyps, primary sclerosing cholangitis and family history of CRC.[210, 211]

FINAL REMARKS

The number of diagnosis of esophageal, gastric and colorectal malignancies is expected to increase in the upcoming years. For these cancers, considering their particular differences, there is a time gap between the premalignant lesion and the invasive cancer. The precursor or early invasive lesion might be identified on an occasional context, as well as in screening or surveillance programs. Endoscopy is fundamental for this early diagnosis and opens a wide field of opportunities for therapeutic interventions.

2. STRATEGIES FOR TRAINING IN ADVANCED ENDOSCOPIC RESECTION TECHNIQUES

INTRODUCTION

High quality training is essential to assure that endoscopy is performed according to the best standards, in order to provide optimal patient care. Medical Societies have produced recommendations for minimum quality performance requirements. Progressively, there has been a tendence in decreasing the importance of number of procedures in favor of the ability to achieve competent and autonomous performance. [6]

Training programs aim to develop knowledge, skills and behaviors in a safe learning environment and enable their transfer into the clinical setting. However, continuous adjustments are required as a response to the fast development of complex endoscopic interventions. Adequate methods, duration and endpoints of training vary greatly and are topics of discussion. Implementation and adherence to these programs is also quite variable.[212]

Despite the increasing efforts to improve training and growing availably of training resources, most endoscopic skills are still learned in real patients, under supervision by a senior endoscopist.

TRAINING PROGRAMS FOR ENDOSCOPIC RESECTION TECHNIQUES

Endoscopic resection techniques, such as ESD and EMR are employed in pre malignant, early neoplastic and subepithelial lesions. In EMR, after submucosal injection, a snare is used to resect the lesion, whereas in ESD after submucosal injection, a mucosal incision around the lesion´s perimeter and gradual submucosal dissection beneath it are performed with an endoscopic knife.[5, 213-215] Modified EMR techniques, such as cap-assisted (a snare is positioned in a specialized transparent cap fitted to the tip of the endoscope) or ligation-assisted (a modified variceal banding kit is used to deploy an elastic band across the lesion of interest), were designed to increase EMR success in specific clinical settings, particularly Barrett's early cancer/high grade dysplasia and subepithelial lesions.[216, 217]

Other techniques such endoscopic full thickness resection are usually reserved for residual, fibrotic lesions, subepithelial lesions and selected early cancers.[218]

When compared to the more invasive surgical approach, these endoscopic treatments allow preservation of the native organ, maintenance of the quality of life and in selected settings, comparable oncologic outcomes, survival and recurrence rates. In addition, costs, duration of the procedure, adverse event rates and hospitalization time are usually lower.[2, 3, 219-221]

The ability to accomplish en bloc resection with EMR is limited to a lesion size up to 20-25mm. Larger lesions removed by this technique imply piecemeal resection and increase the risk of local recurrence.[213, 215]

ESD was conceived in Japan in the mid-1990s, enabling en bloc, R0 resections without size limitation decreasing the recurrence rate and providing detailed histopathologic assessment including lesion´s margins. Comparing to EMR, the risk of adverse events such as bleeding or perforation, procedure time and costs are higher.[4, 9, 10, 21, 222-230]

A learning curve has been observed for clinical successful ESD, reflected by a higher en bloc resection rate, lower procedure duration and fewer adverse events for more experienced endoscopists.[7, 231]

ESD teaching in the East typically occurs under the traditional master-apprentice model, in which procedures are performed on real patients under the supervision of an expert endoscopist.[7, 8]

Although ESD has been extensively implemented throughout Eastern institutions, its adoption by Western countries has been slow. Several considerations have tried to explain it. Some are related to the procedure, like its complexity and requirement for high level of expertise, leading to a steep learning curve; the need for advanced skills in lesion evaluation and selection; the procedure duration; and the adverse event rates. Others pertain to training, such as the lack of qualified ESD experts and training centers (making the learning process under direct supervision not widely achievable) and the lower prevalence of antral gastric neoplasms (decreasing the opportunity to start performing ESD in the easiest and safest location). Finally, general factors, namely the limited access to endoscopic devices, the lack of proper reimbursement and the underestimation of the need and benefit of ESD may also play an important role. Furthermore, Eastern endoscopists, unlike Western ones, have different clinical background, as well as technical experience and typically dedicate themselves almost exclusively to ESD.[4, 5, 12, 13]

Bearing in mind the complexity of ESD, the steep learning curve, the differences between East and West along with the identified barriers for its implementation, a specific, rigorous training program is recommended before ESD is employed in the clinical setting.

Training programs for endoscopic resection techniques and particularly for ESD have focused on (i) baseline endoscopic experience, (ii) acquiring theoretical knowledge, (iii) visiting centers with high ESD volume (observing and assisting procedures), (iv) training with animal models and subsequently (v) starting clinical practice in selected lesions, ideally under supervision of experts.[5, 12, 13, 232] Figure 5 presents a proposal of an algorithm.

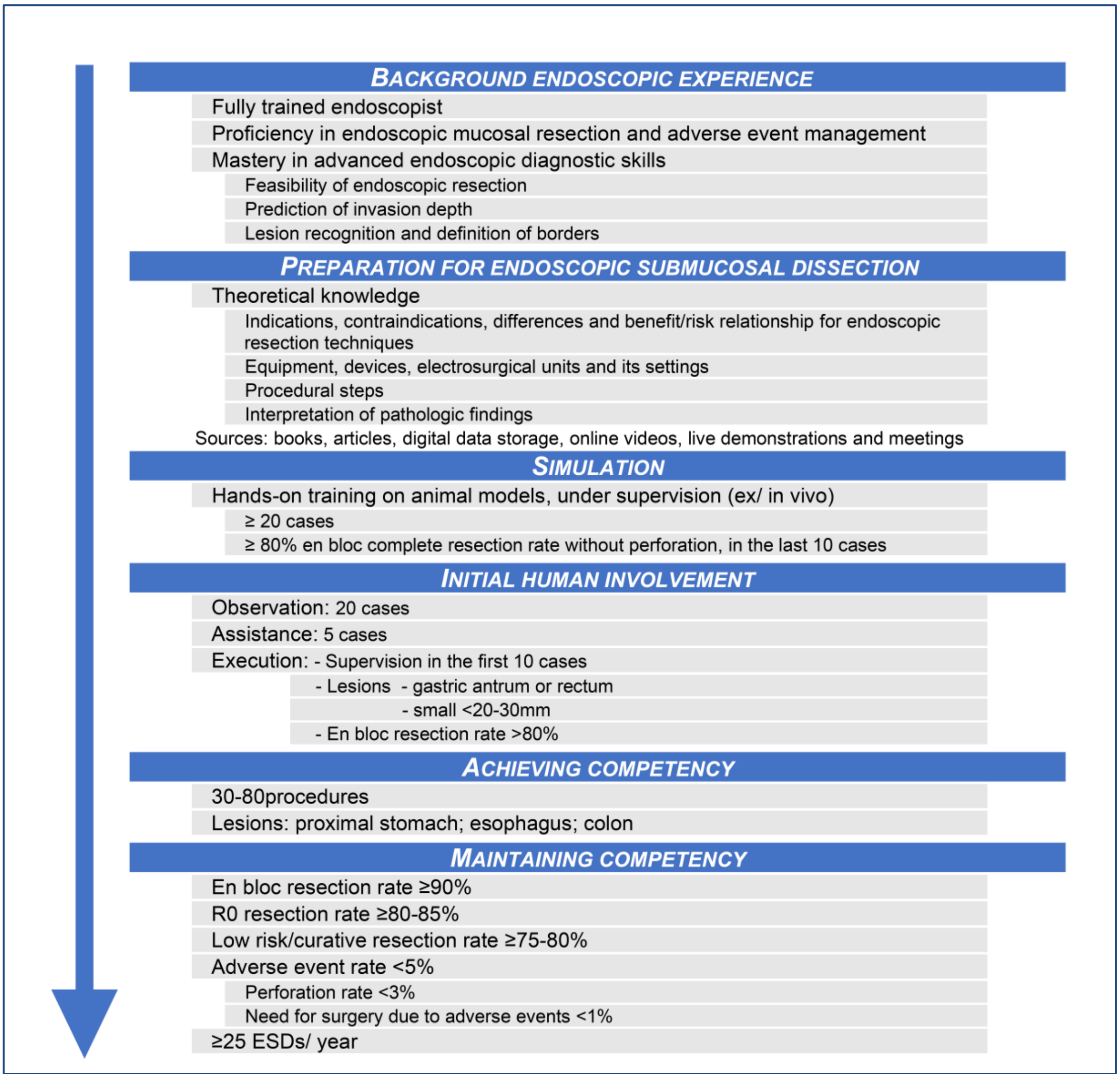

Figure 5. T*raining algorithm for endoscopic submucosal dissection.*
Adapted from [12, 13] [232]

BACKGROUND ENDOSCOPIC EXPERIENCE

Regarding previous endoscopic experience, it is recommended that in the West, a ESD learner should be a senior, fully trained endoscopist with solid endoscopic background in diagnostic and therapeutic endoscopy, proficient in EMR and adverse event management.[5, 12, 13, 232]

Advanced endoscopic diagnostic skills are required and should be mastered before initiating ESD training. A high quality endoscopy is recommended, ideally with contrast or digital chromoendoscopy, by an experienced endoscopist, to establish the feasibility of endoscopic resection, to predict invasion depth and to correctly recognize and define the lesion´s borders.[5, 12, 13, 232, 233] It is essential to assess lesion´s surface morphology, using the Paris classification and for colorectal lesions the laterally spreading tumor classification. Signs of deep invasion such as non-lifting sign, ulceration, friability/spontaneous bleeding, chicken skin sign, folds fusion/convergence, induration, markedly elevated margins and non-extension sign should also be noticed. Surface pattern evaluation, applying optical diagnosis through image-enhanced endoscopy classification systems scales, must be employed. Examples include the Barrett's International NBI Group (BING), BLI New Classification (BLINC) and the Portsmouth acetic acid classification (PREDICT) for BE. The Japan Esophageal Society (JES) classification, the intrapapillary capillary loop (IPCL) classification such as the Inoue and the Arima classifications are used in squamous cell carcinoma. The "vessel plus surface" (VS) classification and the simplified Narrow band imaging (NBI) classification are useful for early gastric cancers. The Narrow Band Imaging International Colorectal Endoscopic Classification (NICE), the Japanese Narrow Band Imaging Expert Team (JNET) Classification, the Kudo Pit Pattern Classification, the Hiroshima Classification and the Sano Classification are utilized in early colorectal cancers.[233-236]

Therefore, determining the appropriate lesions for which ESD is indicated is crucial. In fact, ESD with curative intent is only achievable for unequivocal neoplastic lesions that lack characteristics of deep invasion.

ESD trainees must have excellent handling and precise control of the endoscope. To assure more accurate movements, it is advisable to master right/left angulation controls of the endoscope with the left hand, to rotate the shaft using the left wrist/arm and to use right hand to insert/retract the scope while supporting rotation of the shaft.[237, 238]

Proficiency in EMR and adverse events management is strongly recommended. Experience in hemostatic techniques for active bleeding is important due to the fact that most of the difficulties during ESD practice and training are related to hemorrhage. A trainee must be also prepared to address potential perforations and must be familiar with different closure techniques.[5, 12, 13, 232, 239]

PREPARATION FOR ENDOSCOPIC SUBMUCOSAL DISSECTION

Trainees must acquire theoretical knowledge on indications, contraindications and differences in the available endoscopic resection techniques. Understanding the benefit/risk relationship of ESD when compared to other alternatives, including conventional EMR, precut EMR, hybrid ESD and surgery is also essential.[240] The available resources include books, articles, DVDs, online videos, live demonstrations, meetings, and attendance of ESD procedures performed by experts.[241]

An ESD learner should be familiar with common equipment such as distal attachments, injection agents, knives (needle-type, insulated-type), water jet functions, hemostatic, traction and closure devices along with the characteristics of electrosurgical units and its settings.[232, 240]

All the procedural steps should be understood, namely marking lesion´s border, performing dynamic and sequential submucosal injections to elevate the target area, cutting the mucosa peripherally, performing submucosal dissection, coagulating vessels, retrieving the specimen, exploring the resection bed, performing prophylactic vessel coagulation in the ulcer bed, closing the defect when necessary, pinning adequately the specimen and submerging it in a container with a fixation solution. Awareness of possible adverse events and knowledge on how to deal with bleedings and perforations is essential.[5, 12, 13, 232] It is also important to learn different ESD strategies, like the conventional, pocket and tunnelling methods, along with proper use of gravity, traction or underwater techniques.[237, 238]

The endoscopist should be able to correctly estimate the probability of performing a curative resection based on the endoscopic assessment of the lesion. He must adequately interpret pathologic findings and understand resection outcomes classified in low risk ("curative"), local risk or high risk ("non-curative") resections.[5, 214]

Before implementing ESD, it is crucial to assure the existence of proper endoscopic facilities, as well as access to hospitalization, emergency surgery and expert gastrointestinal pathology.

Registry of ESD procedures in prospective database centers has been suggested.[13, 232, 240]

INDICATIONS FOR ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTROINTESTINAL NEOPLASMS

GENERAL CONSIDERATIONS

Multidisciplinary teams, incorporating knowledge in radiology, endoscopy, medical oncology, surgery, radiotherapy, pathology, nursing and other relevant fields, as required, should determine the adequate treatment proposal for each patient. The role of endoscopic resection is dependent on clinical stage and on the integration of patient-related factors (such as personal preferences, performance status, comorbidities), endoscopy-related factors (such as endoscopic facilities and expertise) and lesion-related factors.[242-250]

ESD provides accurate histologic evaluation, allowing assessment of submucosal invasion, lymphovascular involvement, margins status, degree of differentiation and tumor budding. Importantly, it is considered an adequate treatment option for patients with early GI cancers with no or limited submucosal invasion, no additional risk factors and thus a very low likelihood of lymph node metastasis. In these circumstances, a low risk/curative resection is assumed, precluding the need for surgical intervention and lymph node dissection.[5, 214] Even in cases presenting high risk histopathologic features, ESD may be regarded as a precise staging procedure.

The difficulty of performing ESD is different according to the location of the lesion in the GI tract. The least demanding is the distal stomach, followed, in order of increasing complexity and risk, by the proximal stomach, rectum, esophagus, right colon, transverse, left colon, and duodenum.[13]

The role of ESD is dependent on the lesion´s organ, histological type (SCC vs adenocarcinoma), location within organ (colon vs rectum), size, access and relevance of precise histopathologic assessment.

Guidelines from Japan, Europe, United States of America and from other origins have been issued and updated.[5, 165, 166, 214, 251-257] Indications for ESD in esophageal SCC and gastric adenocarcinomas usually reflect curability/risk resection criteria. Alternatively, in BE and colorectal cases, the process is typically based on lesion detailed assessment to select those for which accurate histopathologic evaluation is clinically relevant (suspicion of limited submucosal invasion) or those for which fibrosis implies an inadequate resection by EMR (table 1).

Endoscopic ultrasonography (EUS), computed tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography-CT (PET-CT) have limited value in the routine assessment prior to endoscopic resection. However, they may be considered in selected cases of esophageal (EUS) and rectal (EUS and/or MRI) carcinomas when submucosal invasion or lymph node metastasis is suspected.[258-262]

ESOPHAGUS

BARRETT'S ESOPHAGUS

EMR and ESD can be used for endoscopic resection of neoplastic lesions within BE complemented by ablation of the remnant non-dysplastic metaplastic Barrett´s epithelium.

In mucosal carcinoma EMR achieves complete local remission and long term complete remission of 96,3% and 93,8%, respectively with a very low complication rate of 1.5%. Recurrence occurs in 14.5% but in the majority of cases, early diagnosis and endoscopic retreatment is feasible during follow up.[166, 263-265]

EMR is therefore, the preferred endoscopic resection method for small flat HGD/mucosal cancers due to the low risk of lymph node metastases (LNM) and its long term effectiveness.

ESD is reserved for lesions with high suspicion of superficial submucosal invasion or with increased probability of unrecognized invasive component, such as lesion´s size >20mm, bulky/nodular (Paris 0-Is or 0-Ip), depressed (Paris 0-IIc) or poorly lifting. When the index histopathology, on preprocedural biopsy, reveals intramucosal carcinoma (particularly multifocal) or equivocal histologic findings, ESD can be considered. ESD has also been suggested for patients whose previous EMR specimen revealed invasive neoplasia with positive margins or in patients with recurrent/residual lesions (table 1).[5, 165, 166, 214, 251, 252]

En bloc excision allows accurate histologic assessment and reduces local recurrence.

Nevertheless, a meta-analyses of ESD in BE related adenocarcinoma showed an en bloc resection rate of 92,9%, an R0 resection rate of 74,5% and a curative resection rate of 64,9%. The suboptimal R0 and curative resection rates may be related to incorrect endoscopic selection and inaccurate lesion´s delimitation.[266]

When EMR and ESD were compared, ESD achieved earlier and higher proportion of complete remission of dysplasia, lower recurrence/residual disease rates, lower need for repeat endoscopic treatments, although similar complete remission of intestinal metaplasia.[267-269]

A low-risk/curative resection is assumed when a superficial lesion in BE is removed en bloc, displaying a histological R0 resection, up to well-moderately differentiated adenocarcinoma, limited to muscularis mucosae (m3) layer and no lymphovascular involvement. When submucosal (sm) invasion is limited to sm1 (≤500mm in BE adenocarcinoma) layer, additional therapy can be considered.[5, 214, 251]

SQUAMOUS CELL CARCINOMA

Esophageal SCC carries an increased probability of LNM at similar stages, compared to BE related neoplasia. For m3 and sm1 (up to 0,200mm in SCC and to 0,500mm for BE adenocarcinoma) invasive lesions, the risk of lymph node involvement is 0 to <2% in BE related adenocarcinoma and 10%-20% in SCC.[167, 270-274] Therefore, one of the main goals of SCC endoscopic resection is en bloc removal to allow accurate histopathologic evaluation.

In lesions <10mm, en bloc EMR may be an acceptable option. Generally, ESD is considered the first line therapy due to the higher en bloc, R0, curative resection and lower recurrence rates. Besides relying on pre procedure diagnosis to exclude major submucosal involvement , the Japanese guidelines introduce the limit of 50mm of major axis length, in lesions with circumferential involvement (table 1).[5, 214, 251, 252]

For SCC, en bloc resection rates of 83%-100%, complete resection rates of 78%-100% and local recurrence rates of 0%-2.6% have been reported.[273-280]

A low-risk/curative resection is assumed when a superficial SCC is removed en bloc, displaying a histological R0 resection, up to well-moderately differentiated carcinoma, limited to lamina propria (m2) layer and no lymphovascular involvement. When invasion extends to m3 layer and particularly to sm1 (≤200μm in SCC) layer, the risk of LNM increases and additional therapy is advised.[5, 214, 251]

STOMACH

Classic absolute indications for gastric endoscopic resection include lesions with LGD/HGD, of any size and differentiated mucosal adenocarcinoma, ≤20mm in size and without ulceration. EMR is an acceptable option for lesions smaller than 10mm-15mm. Differentiated mucosal adenocarcinomas, >20mm in size, without ulceration or ≤30mm in size with ulceration and undifferentiated mucosal adenocarcinoma, ≤20mm in size, without ulceration compose the expanded indications. Recently, the Japanese guidelines also included these lesions in the absolute indication criteria. Differentiated adenocarcinoma, ≤30mm in size, invading sm1 (<0,500mm in gastric adenocarcinoma) layer, complete the expanded indications (table 1).[5, 214, 253, 254]

The histologic nomenclature is not uniform in different guidelines regarding undifferentiated, poorly differentiated, diffuse type, poorly cohesive and signet ring cell carcinomas, which relate to distinct categorizations reported in the Lauren, Nakamura, Japanese Gastric Cancer Association (JGCA) or World Health Organization (WHO) classifications.[5, 214, 253, 254, 281]

In the Japan Gastroenterological Endoscopy Society (JGES) guidelines, papillary adenocarcinomas and predominantly well to moderately differentiated tubular adenocarcinomas are classified as differentiated type cancers, whereas gastric cancers that predominantly include poorly-differentiated adenocarcinomas, signet ring cell carcinomas or mucinous adenocarcinomas are classified as undifferentiated type cancers.[253, 254]

The incidence of LNM for patients fulfilling the absolute indication criteria varies from 0.2% to 0,3%, whereas for patients who meet the expanded indication criteria varies from 0.4% to 0.7%. Whitin this group, undifferentiated, mucosal lesions ≤20mm and differentiated, sm1 invasive lesions, <30mm pose the higher risk, achieving a LNM between 2,5% and 3.0%.[282-284]

ESD compared to EMR achieves en bloc resection rate of 94.5% to 92% vs 66.8% to 52%, R0 resection rate of 92% to 82% vs 48.2% to 52% and recurrence a rate of 0.2% vs 6%.[285-288]

A very low-risk or low-risk/curative procedure is assumed when a superficial gastric lesion is removed en bloc, displaying a histological R0 resection, fulfilling the characteristics for absolute or expanded indications, respectively. Consideration for additional surgery is advised for patients presenting diffuse-type carcinomas, even if satisfying the corresponding expanded indication.[5, 214, 253, 254]

DUODENUM

EMR is the preferred technique for non-malignant duodenal lesions. Large lesion can be effectively removed by piecemeal EMR with a complete resection rate of 96% to 91% and adverse events reaching 24% to 2%.[289-295]

Duodenal location is considered the most challenging for ESD in the GI tract and is associated with a high rate of adverse events, even in experienced centers. Bleeding and perforations, whether immediate or delayed, occur in 13% up to 50% of cases.[296-299]

Duodenal ESD should be limited to highly selected lesions and performed by endoscopists with great expertise.[300]

COLON AND RECTUM

The majority of colorectal lesions, irrespective of size, can be effectively removed by polypectomy/EMR/piecemeal EMR with curative intent.

Colonic lesions >20mm require piecemeal EMR, increasing local recurrence risk up to 15%-30%, which can be reduced to 5% by thermal ablation of the post-EMR mucosal defect margin. Long term success can reach approximately 95% provided adequate surveillance to address potential recurrence/residual tissue.[230, 301-307]

Identification of patients that most likely benefit from ESD should be accomplished through lesion assessment and risk stratification.[302, 308] These lesions contain high suspicion of superficial submucosal invasion or present increased probability of unrecognized invasive component, such as laterally spreading tumors (LST) non-granular (particularly pseudo depressed) >20mm, LST granular nodular-mixed >30mm, lesions with a depressed (Paris 0-IIc) or complex morphology (Paris 0-Is or 0-IIa+0-Is), with type Vi Kudo pit pattern, Japanese Narrow Band Imaging Expert Team (JNET) 2B classification and 3a Sano vascular pattern. Patients with certain lesions that otherwise cannot be optimally and radically removed by snare-based techniques, such as those with submucosal fibrosis, may also benefit from ESD. Examples include lesion with previous biopsy related or peristalsis related fibrosis, lesions in a chronic inflammatory background (such as in inflammatory bowel disease) and local residual/recurrent lesions after previous endoscopic resection (table 1).[5, 214, 252, 255-257]

Such selected lesions, located in the colon, should be highly considered for ESD. Nevertheless, its benefits have to be balanced against the increased procedure risk, the endoscopist experience, as well as lesion´s location and access. Patient age, co-morbidities and preferences must also be taken into account. When lesions with similar characteristics are located in the rectum, the threshold for performing ESD should be lower and it should be considered the first line treatment. This is due to the fact that rectal lesions present a higher risk of submucosal invasion, are easier to access and rectal ESD is associated with a lower adverse event rate. In addition, surgery as a therapeutic alternative or as a rescue therapy (after eventually non-curative piecemeal EMR), carries greater morbidity and stoma risk.

A low-risk/curative procedure is assumed when a superficial colorectal lesion is removed en bloc, displaying a histological R0 resection, up to well-moderately differentiated adenocarcinoma, limited to sm1 (≤1000mm in colorectal adenocarcinoma) layer and no lymphovascular involvement.[5, 214, 255-257]

Table 1. ***A proposal of indications to perform endoscopic submucosal dissection.****

ORGAN/ CONDITION	CHARACTERISTICS OF LESIONS FOR WHICH ENDOSCOPIC SUBMUCOSAL DISSECTION IS INDICATED	
ESOPHAGUS		
BARRETT'S ESOPHAGUS	*Particularly if size >20mm*	
	Suspicion of superficial sm invasion *or* *Increased probability of unrecognized sm invasive component*	- *Size* - >20mm - *Surface morphology* - Bulky / nodular (Paris 0-Is or 0-Ip) - Depressed morphology (Paris 0-IIc) - Poorly lifting - *Index histopathology (on preprocedural biopsy)* - Mucosal carcinoma (particularly multifocal) - Equivocal - EMR specimen displaying invasive neoplasia with positive margins
	Inadequate for snare-based resection (submucosal fibrosis)	- Recurrence/residual
SQUAMOUS CELL CARCINOMA	*Particularly if size >10mm*[†]	
	Absolute indications	- m1-m2; non-circumferential; without size limitation - m1-m2; circumferential; ≤50mm
	Expanded indications	- m3 or sm <0,200mm; (non-circumferential)
STOMACH		
	Particularly if size >10 - 15mm[‡]	
	Absolute indications	- LGD/HGD, without size limitation - ADC, m, differentiated[§], ≤20mm, without U
	Expanded indications	- ADC, m, differentiated[§], >20mm, without U[#] - ADC, m, differentiated[§], ≤30mm, with U[#] - ADC, m, undifferentiated[¶], ≤20mm, without U[#] - ADC, sm invasive <500mm, differentiated[§], ≤30mm
COLON AND RECTUM	Colon - selected cases** Rectum - general rule	
	Particularly if size >20mm	
	Suspicion of superficial sm invasion *or* *Increased probability of unrecognized sm invasive component*	- *Surface morphology* - LST-NG (particularly pseudodepressed), >20mm - LST-G, nodular-mixed, >30mm - Depressed morphology (Paris 0-IIc) - Complex morphology (Paris 0-Is or 0-IIa+0-Is) - *Surface pattern* - Type Vi Kudo pit pattern - JNET 2B classification - 3a Sano vascular pattern
	Inadequate for snare-based resection (submucosal fibrosis)	- Previous biopsies related fibrosis - Peristalsis related fibrosis - Chronic inflammation (Inflammatory bowel disease) - Recurrence/residual

*Adapted from [5, 165, 166, 213-215, 251-253, 257]

ADC, adenocarcinoma; EMR, endoscopic mucosal resection; G, granular; HGD, high-grade dysplasia; JNET, Japanese Narrow Band Imaging Expert Team; LGD, low-grade dysplasia; LST, laterally spreading tumor; m, mucosal layer; NG, non-granular; sm, submucosal layer; U, ulceration.

[†] EMR is an acceptable option for lesions smaller than 10mm, if en bloc resection assured.
[‡] EMR is an acceptable option for lesions smaller than 10mm.
[§] Differentiated: papillary adenocarcinomas and well to moderately differentiated tubular adenocarcinomas.
[¶] Undifferentiated: poorly differentiated adenocarcinomas, poorly cohesive carcinomas (including signet ring cell carcinomas) and mucinous adenocarcinomas.
[#] Considered absolute indications for the Japan Gastroenterological Endoscopy Society.
** According to patient (age, co-morbidities, preference) and procedure risk (endoscopist expertise; lesion location and access).

SIMULATION

Initial ESDs should not be performed in humans. The complexity and potential serious adverse events of the procedure were demonstrated in a study where beginning of ESD was carried out in human rectal lesions. The initial perforation rate was 34% and the initial en bloc resection rate 52%.[309] Therefore, simulation, as an alternative option for initial training, should be sought.

In medical simulation, a situation or environment is created, allowing standardizing of patients, technical procedures execution and clinical scenarios reproduction, in order to represent the real event.[310-312] Learning, practicing, evaluation, testing or gaining understanding of systems and human actions is possible.[313] Cognitive, psychomotor or behavioral skills can be taught to improve the performance of healthcare providers, healthcare processes and eventually patient outcomes.[314-321] Applications for simulation in Medicine are related to (i) improving *patient safety* and *quality programs* (instead of practicing on real patients, such as training in crisis events or novel/infrequent interventions), (ii) *skills training* and *competency assessment*, (iii) *improving clinical teaching constraints* (as an alternative solution to many of the challenges of contemporary medical education) and (iv) supporting the development of *interprofessional collaborative practice*.[322-324]

Simulations continue to achieve widespread acceptance, but several factors limit or challenge its use. Operationalization and participant engagement factors are the most common. Operational issues include the cost of simulation, the need for skilled trainers, along with the time and complexity related to its design, preparation, implementation and evaluation.[325] Participant engagement barriers are consequences of finding the simulations stressful and intimidating or are related to failure of the simulators or trainers to accomplish the intended goals. This has unfavorable implications for learning and influences the experiences of other trainees.[326, 327]

The mentor-apprenticeship model has been the traditional route of endoscopy skills teaching, in which trainees learn under direct supervision of trained endoscopists, in the clinical setting.[25] This clinical training is associated with specific disadvantages, such as the necessity of the preceptor to completely resign control of the endoscope (to allow the trainee to learn), the time increase in each procedure (with capacity and economic implications), the limitation by clinical demands and time restrictions, the determination of exposure by patient encounter (limiting contact to pathology prevalence), the challenges in patient comfort and safety, as well as the increased difficulty to process feedback in a new, potential stressful situation.[25, 328, 329]

Endoscopic simulators, on the other hand, provide the option of teaching diverse competencies in a low-risk, stress-free, controlled environment. The remaining advantages are the opportunity for a sustained, repetitive practice until mastery, the possibility of errors performance without adverse consequences, the individualized learning process (with simulation tasks adaption), the fact that trainers may focus exclusively on learners (instead of struggling between teaching and clinical demands), the option of exposure to potential infrequent, specific clinical conditions or techniques and the possibility of skills maintenance in case of interrupted clinical practice.[25, 330-332]

Some studies have demonstrated that simulation-based education improves endoscopic process skills in test setting and in clinical practice, as well as in patient outcomes, compared with no intervention.[22] Evidence on the use of simulators is available on the early training phase by shortening the learning curve to competency and mainly for validated virtual reality simulators.[23-26] However data on the assessment of performance or competence levels in patient-based endoscopy are lacking.

Mechanical simulators are composed of inanimate tissue materials, intended to mimic anatomic structures where motor tasks are performed with a real endoscope. They are associated with lack of realism with inadequate simulation of tissue properties.[26, 333] In virtual reality computerized simulators, endoscopes are maneuvered within a virtual intraluminal scenario by hardware components and software functionalities. Although able to provide real-time feedback, various clinical cases, standardization of training and generating metrics for evaluation of users performance, when addressing complex therapeutic interventions, such simulators are not ideal. This is due to the inability to reproduce the tissue properties, such as elasticity and tactile feedback of human tissue.[26, 334-337]

Ex vivo and live animal models are deemed more suited for this type of training, considering its human resemblance.

Despite different assessment parameters, ESD performance appears to improve with animal training and supervision during this period is advised.[16, 338-341]

Prior to human ESD start, at least 10 to 30 procedures are recommended in the animal model.[14, 340, 342] Particularly, the European Society of Gastrointestinal Endoscopy (ESGE) suggests a minimum of 20 cases, with 8 en bloc complete resections without perforations in the last 10 procedures.[232]

INITIAL HUMAN INVOLVEMENT

Observing and assisting ESD procedures performed by experts improves procedural skills. It exposes the trainee to different settings, organs and adverse events, increasing its involvement and concentration. Japanese and European recommendations suggest observation of 20 ESD and assistance of 5.[5, 13, 232, 343]

The gastric antrum is the preferred place to start performing ESD due to the easy lifting of the submucosa, straightforward endoscopic access and thick muscularis propria layer. It is therefore recommended to initiate clinical ESD on small lesions of the antrum, without ulceration or scarring. Resection of lesions in the distal stomach is associated with shorter procedure time and perforation, as well as lower procedure difficulty and risk of non-curative resection, compared to more proximal locations.[241, 344]

Considering the scarcity of antral lesions in some Western countries, the rectum has also been considered an alternative location for beginners. The reasons for that relate to the higher incidence of rectal lesions, good maneuverability of the scope and low morbidity of rectal perforations. It is recommended to avoid lesions with fibrosis/scarring, namely in patients who have undergone prior incomplete resections or have ulcerative colitis, as there is a greater probability of increased difficulty. Rectal ESD experience may allow a progressive stepwise approach to the colon with fewer risks.[345-347]

Starting clinical ESD in the colon is not advised, as demonstrated by a R0 resection rate of 58,0% and a perforation rate of 15,5%, by endoscopists with previous animal training, but without gastric ESD exposure.[348] Other reports described perforations rates of 10,0%-12,5% in this setting.[349, 350]

Supervision of an ESD expert endoscopist for the first 10 human procedures is recommended as it offers the opportunity to advise, orally instruct and provide hands-on assistance, if needed.[232, 240, 351]

ACHIEVING COMPETENCY

Case volume as a surrogate for competence is inaccurate, considering the different rates at which trainees acquire specifics endoscopic skills.[351] Additionally, learning curves on ESD are variable, depending on several factors such as the endoscopist experience and training, as well as the organ where the procedure is performed.[12]

Nevertheless, 30 cases has been regarded as the minimum for a beginner to gain early proficiency/competence in gastric ESD.[7, 352]

One study demonstrated that trainees require 40 procedures for successful removal of lesions within the classical indications and 80 cases for lesions within the expanded indications, to achieve outcomes similar to experts.[8] A minimal experience of 20-40 distal gastric ESDs before attempting more proximal areas or extra gastric locations has been recommended,[13, 353] but expertise in gastric ESD was suggested to be attained only after 50-100 procedures in another study.[241]

According to the American Society for Gastrointestinal Endoscopy (ASGE) Guidelines, 30 gastric ESDs represent the minimum number of procedures that should be performed before assessments of competency and/or seeking of credentials/privileges.[354]

Regarding colorectal ESD, for endoscopists with prior gastric ESD practice, 40 procedures were deemed necessary to successfully perform ESD avoiding perforations and 80 to effectively treat large colorectal tumors.[355] Others have reported adequate skill acquisition after 30-50 procedures.[356, 357] In another study, accomplishing >100 procedures was identified as an independent predictor of success and a plateau of high effectiveness and low morbidity was achieved after 120 procedures. [346, 358] In a systematic literature review, procedure speed improved after 30 colorectal cases and acceptable en bloc/R0 resection rate was achieved after 40 cases, for endoscopists with previous ESD experience.[359]

MAINTAINING COMPETENCY

Although competence may not be defined only by number of procedures, a minimum volume is a prerequisite for skill acquisition and sustaining a number of ESDs per year relates with outcome measures and adverse events rate.[351, 360]

Clinical outcomes for Eastern series are generally regarded as better than those from Western ones. These differences seem to be more dependent on case load and endoscopic experience than on endoscopist origin and also more relevant for colorectal than for upper GI ESD.[361, 362]

Available target metrics suggest an en bloc resection rate ≥90%, an R0 resection rate ≥80%-85%, a low risk/curative resection rate ≥75%-80%, an adverse event rate <5% (perforation rate <3% and need for surgery due to adverse events <1%) and a resection speed ≥9cm^2/h.[13, 232, 363]

The threshold value for curative resection rate should account for the following. Increasing expertise may lead to a greater request for ESD in patients whose lesions may be at the borderline for endoscopic treatment, but due to their general health status or preference, may not be surgical candidates. Additionally, the accuracy of distinguishing tumors confined to the mucosa from tumors with slight submucosal invasion is not ideal, even with experts, which may justify performing ESD in such lesions. The result can be a low risk/curative resection, but may also display a non-curative/high risk resection, which at the most, becomes an accurate T staging resection, that will not disturb further additional treatment deemed necessary.[232, 251]

Considering the limitation of procedure numbers to assess competency, maintaining outcome measures at the proposed thresholds should be the target for continuous practice. Nevertheless performing 25 ESDs/year has been suggested, independently of the organ. Still it is important to recognize that, although the general procedural method is similar for different organs, the technical complexity, adverse events, as well as the particular technical details and strategies may be different.[232, 251, 360, 364]

V. SIMULATION IN GASTROINTESTINAL ENDOSCOPY TRAINING

A) THE ROLE OF SIMULATION

SIMULATOR TRAINING IN GASTROINTESTINAL ENDOSCOPY - FROM BASIC TRAINING TO ADVANCED ENDOSCOPIC PROCEDURES.

van der Wiel SE, Küttner-Magalhães R, Rocha Gonçalves CR, Dinis-Ribeiro M,
Bruno MJ, Koch AD.

Best Pract Res Clin Gastroenterol. 2016;30(3):375-387. doi: 10.1016/j.bpg.2016.04.004.

Best Practice & Research Clinical Gastroenterology 30 (2016) 375–387

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology

4

Simulator training in gastrointestinal endoscopy – From basic training to advanced endoscopic procedures

S.E. van der Wiel, MD, Research Fellow [a, 1],
R. Küttner Magalhães, MD, Gastroenterologist, Staff Member [b, 2],
Carla Rolanda Rocha Gonçalves, MD, PhD, Gastroenterologist, Staff Member [e, f, g, 4],
M. Dinis-Ribeiro, MD, PhD, Gastroenterologist, Professor, Head of Department [c, d, 3],
M.J. Bruno, MD, PhD, Gastroenterologist, Professor, Head of Department [a, 5],
A.D. Koch, MD, PhD, Gastroenterologist, Staff Member [a, *]

[a] *Department of Gastroenterology and Hepatology, Erasmus MC – University Medical Center Rotterdam, 's Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands*
[b] *Department of Gastroenterology, Santo António Hospital, Porto Hospital Center, Largo Prof. Abel Salazar, 4099-001 Porto, Portugal*
[c] *Department of Gastroenterology, Portugese Oncology Institute of Porto, Rua Dr. Bernardino de Almeida, 4200-072 Porto, Portugal*
[d] *CIDES/CINTESIS, Porto Faculty of Medicine, Portugal*
[e] *Life and Health Sciences Research Institute, School of Health Sciences, University of Minho, Braga, Portugal*
[f] *Life and Health Sciences Research Institute/3B's – PT Government Associate Laboratory, Braga/Guimarães, Portugal*
[g] *Department of Gastroenterology, Hospital Braga, Portugal*

Abbreviations: *OGD, oesophagogastroduodenoscopy; EMR, endoscopic mucosal resection; EMS, ERCP mechanical simulator; ESD, endoscopic submucosal dissection; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; GI, gastrointestinal; VR, virtual reality.*

* Corresponding author. Tel.: +31 107040045; fax: +31 107030352.

E-mail addresses: s.e.vanderwiel@erasmusmc.nl (S.E. van der Wiel), rkuttner@gmail.com (R. Küttner Magalhães), crolanda@ecsaude.uminho.pt (C.R. Rocha Gonçalves), mdinisribeiro@gmail.com (M. Dinis-Ribeiro), m.bruno@erasmusmc.nl (M.J. Bruno), a.d.koch@erasmusmc.nl (A.D. Koch).

1 Tel.: +31 107033040; fax: +31 107030352.
2 Tel.: +351 22 207 7500; fax: +351 22 3320318.
3 fax: +351 22 5084055.
4 Tel.: +351 253 604 912.
5 Tel.: +31 107035946; fax: +31 107030352.

http://dx.doi.org/10.1016/j.bpg.2016.04.004

376 S.E. van der Wiel et al. / Best Practice & Research Clinical Gastroenterology 30 (2016) 375–387

Keywords:
Endoscopy
Gastrointestinal
Endoscopic procedures
Simulation training
Computer simulation

A B S T R A C T

Simulator-based gastrointestinal endoscopy training has gained acceptance over the last decades and has been extensively studied. Several types of simulators have been validated and it has been demonstrated that the use of simulators in the early training setting accelerates the learning curve in acquiring basic skills. Current GI endoscopy simulators lack the degree of realism that would be necessary to provide training to achieve full competency or to be applicable in certification. Virtual Reality and mechanical simulators are commonly used in basic flexible endoscopy training, whereas *ex vivo* and *in vivo* models are used in training the most advanced endoscopic procedures. Validated models for the training of more routine therapeutic interventions like polypectomy, EMR, stenting and haemostasis are lacking or scarce and developments in these areas should be encouraged.

Introduction

During the last decades simulation-based training has gained more acceptance in teaching basic endoscopy skills to novice endoscopists. Traditionally, trainees learn to perform endoscopy by hands-on training in a clinical setting under the supervision of a trained endoscopist, the so-called master apprentice model. The main benefit of this teaching method is on-the-job training under one-on-one supervision by an experienced endoscopist offering immediate feedback. However, taking the first steps in flexible endoscopy while performing procedures on actual patients has certain drawbacks. It is learning by 'trial and error', which potentially increases patient discomfort and risk of complications. It also adds extra time to each procedure affecting capacity and economics [1]. An important drawback of such an approach is that with this type of training it is difficult for novices to appropriately process feedback in a stressful situation with an overload of new information. The approach of 'see one, do one and teach one' therefore seems outdated and no longer appropriate in the modern education of medical professionals, in particular in their early learning curve. Skillslabs and simulators offer the potential to train in a dedicated 'learning environment'. This is a safe environment for trainees where no possible harm can be done to patients. Stress factors related to doing a procedure in a live patient are eliminated to create an optimal setting for training. In this particular learning environment, it is also entirely possible to combine hands-on training with thorough theoretical teaching. Exercises can be repeated multiple times in small building blocks or specific scenario's until fully mastered.

In recent years, a number of studies have been published on simulator training, usually describing the benefit of simulator training in the early learning curve towards competency. A recent systematic review demonstrated moderate quality evidence for simulator-based training in forward viewing flexible endoscopy and ERCP. The review reveals that the use of virtual reality simulators in the early training setting accelerates the learning of practical skills [2]. However, the literature on simulator training for more advanced therapeutic procedures is scarcer, aside from studies on managing acute gastrointestinal bleeds or advanced endoscopic resection in *ex vivo* or *in vivo* animal models. A realistic simulation model for polypectomy, one of the most frequently performed therapeutic procedures, is still lacking among currently available simulators. Compared to the aviation or automotive industry, we can only acknowledge with envy that we are miles behind when it comes to realistic medical simulators.

In this chapter we will outline the well-established role of simulators in basic endoscopy training and elaborate on the role of (virtual reality (VR)) simulators, mechanical models, *ex vivo* and *in vivo* models for training in advanced endoscopic procedures.

Available simulators

The first simulators for flexible endoscopy were developed in the 1960s. In general there are four types of simulators: 1) mechanical simulators, 2) live animal models, 3) *ex vivo* models and 4) VR computer simulators. The first endoscopic simulators were mechanical models, designed especially for training sigmoidoscopy and colonoscopy. Live animal models seem to be the most realistic compared to mechanical models with haptic feedback resembling that of human tissue, although there are distinct differences in wall thickness and orientation of various organs, resulting in a slightly different 'feel'. Live animal models have certain drawbacks including the costs involved, the fact that they can only be used in specially equipped facilities, that they cannot be used indefinitely, and that many ethical concerns have been raised by the public [4]. A good alternative for live animal models is *ex vivo* models, composite and explanted animal organ simulators. These models consist of a combination of plastic parts and explanted animal organs obtained from slaughterhouses. They overcome some of the aforementioned limitations of the live animal models and have proven useful in specific training scenarios. Currently VR simulators are the most promising tools. They are available plug-and-play, making it accessible for trainees to train at their own pace and procedures can be repeated as many times as desired.

The optimal training model or simulator has to show the highest degree of content validity as well as concurrent validity. This means that the system has a high level of resemblance to the real life activity and that performance on the model should be readily transferrable to the real life activity, *in casu* patient-based endoscopy. Lesser, but more commonly used forms of validity are expert and construct validity. These terms describe the degree of realism as judged by experts and the ability of the simulator to distinguish different levels of competence [3]. The reliability of a simulator relates to its ability to provide consistent results with minimal errors of measurement. The most commonly used test is the test–retest reproducibility. It predicts to what extent a subject can 'beat the test' by repeated assessment [5].

Role of simulators in basic forward viewing flexible endoscopy training

Advanced therapeutic endoscopy has proven itself as an effective and safe first-line treatment for the management of early gastrointestinal neoplasia, pancreatico-biliary disease and many more conditions. Conditions formerly restricted to the domain of surgeons are now managed using minimally invasive endoscopic techniques, not only with considerably less morbidity and mortality, but also superior post-procedural functional results. Moreover, diagnostic endoscopic procedures are gaining importance largely as a result of the initiation of colorectal cancer screening programs in many countries worldwide. As a consequence, the increasing number and in particular the higher complexity of endoscopic procedures demands more skilled endoscopists able to perform these procedures in a competent manner. Simulation-based learning programs have proven to be of added value, they can effectively speed up the learning process in the early stages of training, avoid patient harm and lower one-on-one instructor time. Consequently, the use of simulators in the early training phase in different gastrointestinal procedures is gaining acceptance and several simulators have been validated for this purpose [2,6].

Oesophagogastroduodenoscopy

Oesophagogastroduodenoscopy (upper gastrointestinal endoscopy, OGD) is widely used for the diagnosis and treatment of oesophageal, gastric and small bowel conditions. In general, it is a safe and well-tolerated procedure. A variety of technical and cognitive aspects must be mastered in order to perform a high-quality examination. Although OGD is a common gastrointestinal (GI) procedure, studies concerning simulator-based training are scarce compared to colonoscopy. A possible explanation might be the fact that by gaining competency to perform a colonoscopy, where the need for endoscope handling and manoeuvring is much higher, performing OGD seems relatively easy. Several simulators have been developed for training OGD: mechanical models, *in vivo* and *ex vivo* animal models and VR simulators. The only validated VR-simulator for training upper endoscopy is the 'GI Mentor' virtual reality computer simulator (Fig. 1) [7,8].

Fig. 1. The Simbionix GI Mentor II.

Not much is known about the validation and use of mechanical models for basic training in upper GI endoscopy. Most models appear inappropriate for training as the level of competency gained by the trainee has been negligible [9]. The best known *ex vivo* model is the Erlangen Endo-Trainer [10]. The model is mostly appreciated for training bleeding situations and seems to offer a good training scenario. Validation studies or studies on learning curves are however few. These include three studies that used the 'GI Mentor' VR simulator, to evaluate the learning curve in simulator-based OGD training [11–13]. The main outcome measures in these studies were procedure time and time to reach specific landmarks such as passing the oesophagus and the pylorus and intubating the duodenum. Secondary outcomes were intubation time, movement techniques, procedural success rates and patient outcome such as pain and discomfort. All these studies have shown that simulator-trained participants, compared to controls, have a significantly lower overall procedure time and a significantly improved technical accuracy. The simulator-trained group also appears to operate more independently compared to the controls. The training with these simulators was of no benefit to experienced endoscopists [7,11–14].

The model has an added value in training novice endoscopists, but the effect of training overall seems to be limited. One study showed that the effect of simulation-based training was still visible after the first 60 endoscopic procedures as measured by a shorter procedure time, but not with regards to neither the technical and diagnostic accuracy nor the patients' comfort levels [12]. Another important finding was that performance scores derived from the simulator, did not correlate with performance scores given by blinded experts [15,16]. These findings suggest that the virtual reality simulator training in OGD offers limited added value to patient-based training and only in the very early learning period [12,14,17–19].

Colonoscopy

The use of simulators in colonoscopy training has been extensively studied and remains a topic of ongoing research. Multiple studies have been performed in which mechanical, *ex vivo* and VR simulators have been validated for training colonoscopy [2]. The Kyoto Kagaku Colonoscope Training model is currently the only mechanical model that has been validated. Performance on this model has been shown to correlate well with the level of expertise of endoscopists as measured by caecal intubation in patient-based endoscopy [20]. A validation study using an *ex vivo* bovine colon model demonstrated good construct, expert and concurrent validity. A strong correlation was seen between performance on the model and outcome during patient-based colonoscopy, suggesting the potential of an effective tool for assessment of competency [21]. The most convincing evidence currently available in training

Fig. 2. The Olympus Endo TS-1 VR simulator.

colonoscopy is on VR simulators. Multiple validation studies have been performed, evaluating three different VR simulators; The Simbionix GI Mentor II (Fig. 1), the Olympus Endo TS-1 VR Simulator (Fig. 2) and the CAE Endo VR Simulator, formerly known as the AccuTouch Immersion Medical Computer Simulator [2,7,14,16,17,21–32]. All of these simulators appear to be valid for basic colonoscopy training. Training on VR colonoscopy simulators focusses mainly on intubation skills. There are hardly any data available on training withdrawal skills and mucosal inspection or therapeutic procedures like polypectomy. Most studies had a randomized design, comparing simulator-based training versus no training followed by routine patient-based training or comparing simulator-based training versus patient-based training followed by patient-based assessment [33–42]. It has been demonstrated that simulator training leads to improved performance compared to no training lasting up to the first 80 colonoscopies in humans and that simulator training compared to patient-based training results in equal performance in the early phase of learning. A recent study using the GI Mentor demonstrated increased performance during patient-based colonoscopy after prolonged training on the simulator. After an average of 60 simulator procedures the learning effect on the simulator itself ceased which coincided with observations in patient-based colonoscopy. This tells us that when the learning effect on the simulator stops, the same applies for the transfer to patient-based endoscopy and the time has come to continue training in a human setting. The simulator derived learning effect can probably be extended when the degree of realism of the simulator increases. This observation is a well-known concept in high fidelity aviation simulators [43]. Based on currently available evidence, the effectiveness of simulator-based training in speeding up the early learning curve, thereby reducing patient's burden has been well established. The use of simulators in colonoscopy is therefore strongly recommended prior to performing patient-based endoscopy. To get the most out of simulator training it seems to make sense to train up to the point where the learning effect on the simulator itself levels off. This provides the opportunity to offer tailored training programs to novice endoscopists and determine when to commence patient-based endoscopy on an individual basis.

Role of simulators in advanced endoscopy training

Endoscopic retrograde cholangiopancreatography

Endoscopic Retrograde Cholangiopancreatography (ERCP) is considered an advanced endoscopic procedure and, in most countries, is not part of the routine training of novice endoscopists. It is one of the most technically demanding and high-risk procedures in GI endoscopy. Serious life-threatening short-term and long-term complications may arise as a result of an ERCP procedure, including post-ERCP pancreatitis, bleeding and perforation. It requires a great deal of training and an extensive number of procedures to achieve competency. Nowadays diagnostic ERCP procedures are considered obsolete, meaning that all ERCP procedures are performed with a therapeutic intent. In order to minimize patient risk, trainees need to be properly trained both clinically as well as technically and exposed to high numbers of procedures under the guidance of experts before reaching a status of competency. Simulator-based training seems ideally suited as a training platform for this complex procedure before embarking on real life procedures. Surprisingly, there is very limited data available concerning endoscopic simulators in ERCP training. A total of 6 simulators have been described, including mechanical simulators, a model utilizing *ex vivo* porcine organs, the anesthetized pig model and computer models. Known mechanical simulators with a module for ERCP training include the X-Vision ERCP Training system and the ERCP Mechanical Simulator (EMS) [44,45]. These models are made out of aluminium, plastic and rubber components, with either a synthetic or *ex vivo* papilla and provide the possibility to train with real endoscopes and accessories. Selective bile duct or pancreatic duct cannulation can be practised with selective stent placement, balloon dilatation, brush cytology and, in some, sphincterotomy. Practising stone extraction has not been described in any of the models. Primary outcome parameters in studies evaluating the mechanical model are successful selective cannulation of the biliary duct and the time required to complete several procedures. Both models are able to distinguish between novice endoscopists and experienced endoscopists by means of expert assessment. After a short mechanical simulator training course a higher number of successful cannulation rates was seen in simulator-trained participants in patient-based ERCPs [45–48]. This improved performance was only described for the first 25 consecutive procedures in humans as follow-up time was limited. Live anesthetized porcine models also have been used as a model for ERCP training. This model has been shown to be adaptable to all procedural aspects of ERCP including cannulation, stent placement and sphincterotomy. After a two-day hands-on training course participants showed an increase in confidence scores, especially in performing more complex procedures like needle-knife pre-cut sphincterotomy [49,50]. Puzzlingly, confidence in performing basic skills did not increase. The Erlangen Endo Trainer can also be equipped with an ERCP module, consisting of an *ex vivo* porcine stomach model with attached biliary system. It allows trainees to train with a real endoscope and accessories. The model has been extensively used in ERCP training workshops [51,52]. The Erlangen Endo Trainer, as well as the live animal model, scored high on realism and the model seems most useful in teaching basic ERCP skills [10,52]. The only validated VR endoscopy simulator in ERCP is the Simbionix GI Mentor II VR Simulator. The model is able to differentiate between novices and experts in time to complete procedures and time to reach the papilla; however the model received a low score for realism [53]. Recently, a study was performed using the CAE Endo VR Simulator. This simulator provides a platform for training in diagnostic procedures, however it seems not to be useful in measuring change in performance over time and assessing competency [54]. Sedlack et al. performed a comparison validation study including the Erlangen Endo Trainer, the live porcine model and the GI Mentor II. The study concluded that each model has the potential to be included in training programs; however the Erlangen Endo Trainer scored highest on indices of realism, usefulness and performance. The GI Mentor II scored significant lower at indices of realisms but is easier to incorporate in a training program [52]. The most common performance parameter in simulator-based training in ERCP is successful cannulation rate. This measure reflects only part of the complexity and diversity of this therapeutic procedure. A successful biliary cannulation is a prerequisite to complete a therapeutic procedure successfully but is not a good predictor for successful ERCP procedure. All of these simulators show definite training potential, but based on the scant scientific data available, a definite recommendation for a well-described training program cannot be provided.

Endoscopic ultrasound

Since the description of the first transgastric pancreatic pseudocyst drainage using a linear echo endoscope by Grimm et al., endosonography (EUS) has rapidly changed from a mere diagnostic tool to a technique with advanced therapeutic capabilities [55]. Notably, the advanced EUS therapeutic procedures have a marked overlap with ERCP and demand a great deal of expertise and experience. Although the need for highly skilled endoscopists is obvious, validated simulators or models for training are lacking. There are only a few reports on simulator-based training in EUS. A learning effect by repeated exercise and improvement of performance during EUS procedures in the live porcine model was demonstrated by Barthet et al. but no formal attempts at validation or transfer of competence to a patient-based setting have been made [56]. Advanced endoscopic resections such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are typically trained in a simulator-based setting using animal models. Both *ex vivo* and *in vivo* models are used. The *ex vivo* model is mostly used for training bleeding complications. These topics are discussed in a separate paragraph below.

Advanced therapeutic procedures

Simulator-based training has demonstrated its use in training the basic skills in GI endoscopy. However, as GI endoscopy is no longer a merely diagnostic procedure, this obviates the need for training an increasing diversity of advanced therapeutic procedures outside the standard clinical scenario. Unfortunately we must acknowledge that there is very limited evidence to support training of these procedures in a skillslab environment. Standard polypectomy or endoscopic mucosal resection (EMR) are perfect examples of techniques that currently cannot be trained in any of the models or VR simulators with a degree of resemblance that comes close to the real thing. A few studies using the Erlangen Endo Trainer have demonstrated a positive effect of simulator-based training for certain interventional skills like endoscopic haemostasis and perforation closure. Haemostasis was simulated using several techniques and a significant improvement has been documented in performing successful injection or coagulation therapy [4,10,57]. The transfer of these skills to patient-based endoscopy and its impact in real-life practice is usually not described, so from a scientific point of view we cannot conclude that training in these models is useful. However, as these training scenarios closely resemble the clinical setting, using the same instruments, it seems common sense that training in these models will at least partially improve the skills necessary to apply these techniques.

Advanced endoscopic resections

Pre-malignant and early neoplastic lesions are commonly detected in clinical practice. Interventional endoscopy, namely endoscopic submucosal dissection (ESD) and complex endoscopic mucosal resection (EMR) have replaced surgery for the treatment of many of these conditions. EMR of large lesions can be technically demanding and allows for *en bloc* resection of lesions up to 20–25 mm. Lesions larger than this typically require piecemeal EMR which can complicate histological staging in some settings and can be considered a limitation regarding early cancers, depending on the location in the GI tract [58]. In these situations, ESD seems to be the resection technique of choice, but it is technically more challenging and has a more prolonged learning curve [59–62]. In the appropriate setting, ESD is comparable to surgery in terms of oncological outcomes, cancer free survival and recurrence, but with considerably lower costs, operative time, hospital stay, complication rates and mortality [63]. ESD had a widespread dissemination in Eastern countries but a relatively slow diffusion in Western countries due to its complexity, the requirement for considerable endoscopic skills, the high potential of serious adverse events and the difficulty in achieving adequate funding for these complex endoscopic procedures. A learning curve in performing successful ESD procedures has been demonstrated, and more experienced endoscopists have higher rate of *en bloc* resection, reduced procedure duration and fewer adverse events, mostly related to perforations [64,65]. Therefore, a pre-patient training program is recommended before ESD is performed in the clinical setting [64,66,67]. The differences between the East and West support the use of simulators for ESD training in the West, whereas in the East, where expert supervision and suitable learning cases are easily available, a simulator phase may not be necessary [68]. Pure mechanical simulators and VR simulators are not ideal when addressing advanced endoscopic resection training, due to the inability to reproduce the elasticity, tissue properties and tactile feedback of human tissue [69]. Workshops with animal models are being organized in many specialized training centres with the potential to aid in speeding up the learning process and achieve initial competence in ESD in a safe learning environment with direct one-on-one expert supervision. This is especially relevant where there are few adequate cases in clinical practice, and expert supervision is not readily available or hard to organize [70–72]. Simulation with explanted animal organs like the oesophagus, stomach and colon, facilitates the execution of therapeutic endoscopic procedures in a more realistic fashion with lower costs compared to mechanical simulators [73]. *Ex vivo* models have the advantage of being easy to assemble, more affordable and raising less ethical issues when compared to live animal models. On the other hand, the *ex vivo* model lacks a certain degree of realism due to its inability to bleed, although modifications can permit simulated blood flow and bleeding [64,73–75]. Harvested organs can be attached to insertion tubes or assembled in plastic models, thus oesophageal, gastric and colonic models are available [76–79]. The Erlangen Active Simulator for Interventional Endoscopy (EASIE) was the pioneer and is the best known model, in which explanted organs are mounted in a human shaped plastic torso [80]. It has been suggested that *ex vivo* models cannot substitute *in vivo* training to acquire competence in ESD because even fresh cadaveric animal tissue is stiffer and generally more robust than live human tissue which alters the ESD technique. It is advised that learners proceed to live animal models soon after acquiring adequate basic ESD skills on explanted organs [72,74]. Animal models, generally anesthetized pigs, have breathing movements, heart beats, peristalsis, intraluminal secretions, tissue reaction to injection and electrocautery, and abdominal distension which more closely resembles the human setting. It is possible to deal with adverse events, such as bleeding and perforation in a more realistic setup. Usually, the submucosal injection is more difficult compared to human cases, with a lesser degree of bleeding, and often more fibrosis. The orientation of various organs can be different and pathological scenarios are generally difficult to be reproduced [64,71,74,81]. The thickness and stiffness of the gastric porcine mucosal layer appears to be different from the human stomach [82]. In fact, mucosal layer in this model is thinner in the proximal stomach and thicker in the distal area, particularly at the level of the greater curvature, where ESD is more challenging than in a similar human procedure. It has been suggested that the greater curvature, particularly the distal part of the porcine stomach is the least suitable place for ESD training [83]. Initial attempts ought to be in the gastric antrum and then progress can be made to more proximal regions of the stomach and other organs such as the oesophagus or colon [70,76,78]. Validity and clinical benefit of training ESD in this model and subsequent complication management has not been well established and is currently being investigated by our study group. Nevertheless, by training in the animal model it is possible to recognize a learning curve regarding procedure time, completeness of procedures and adverse events. A study demonstrated that the mean resection time was significantly decreased for porcine gastric ESDs in the second half of the study cases [71]. In another study, two novice endoscopists were able to decrease procedure times, perforation rate and achieve 100% *en bloc* resection after accomplishing 30 gastric ESDs in an *ex vivo* porcine model [77]. The rates of endoscopic closure for colorectal perforations by two non-experts increased from 40 to 60% in the first five cases compared to 100% in the last five procedures [75]. Lastly, four endoscopists without any ESD experience were able to perform uneventful human gastric ESD after training in *ex* and *in vivo* animal models, thereby demonstrating the transfer of skills to a patient-based setting [72]. Based on the few studies that are available on this subject, a minimum of 10–30 gastric ESD procedures in the animal model should be recommended before moving to human cases [77,84,85]. Performing ESD in the oesophagus is more demanding than gastric ESD. This is in part due to the thinner muscle layer and the tubular shape of the oesophagus which provides a limited space to work in [67]. It has been demonstrated that by training in *ex vivo* models for oesophageal ESD, endoscopists with experienced in gastric ESD, were able to reduce the operation time and the number of deep injuries to the muscularis propria after 10 procedures, when the five initial ESDs were compared to the final five [76]. Colorectal ESD is technically the most demanding. Difficult positioning and an increased risk for adverse events, mostly perforations, make it particularly challenging, even for the expert endoscopist. Training is therefore essential and animal models may play an essential role [74,86]. Live animal models for colorectal ESD are difficult to prepare as it requires adequate bowel preparation before attempting any procedure. For colorectal ESD training, porcine and bovine *ex vivo* models have demonstrated their feasibility [75,79]. In a study using an *ex vivo* model for colonic ESD, technical proficiency increased over 10 procedures. In the first two cases, incomplete resections and perforations occurred, whereas in the following cases procedure time decreased and no further adverse events occurred [78].

A glance at the future

Numerous simulators have been developed over the last decades. The aim of simulator-based training is to provide a platform for training in a specialized learning environment and the possibility to repeat procedures in order to gain competence before performing patient-based endoscopic procedures. Ideally, this reduces patient's burden and results in well-trained, well-prepared and to some extent competent endoscopists. Current simulators, whether (VR) simulators, *ex vivo* or *in vivo* models, are still lacking the degree of realism that would be necessary to achieve full competency at a level where certification could be applicable. The conclusion of a large overview of our current state is that simulators have proven their value in training novice endoscopists through their first steps in the world of flexible endoscopy. As well as at the far end of the spectrum, where they can be used to train a select group of experienced endoscopists in advanced endoscopic resection techniques. The large part in between seems to be void. The best example is the standard polypectomy training. A simulation-based scenario is not available for this kind of rather routine procedures, which however incur risks of adverse events and which is performed by virtually all endoscopists. Future research is needed to focus mainly on common therapeutic interventions such as polypectomy and EMR of sessile polyps up to 2 cm, stricture dilatation, stent placement and bleeding scenarios like variceal bleeds using rubber band ligation or endoscopic therapy for ulcer bleeds. Studies should focus on validating and improving the performance of the models, but also on the transfer of skills to patient-based settings, a step that is often omitted but that is in fact the only proof of concurrent validity. Another vast area in the broad arsenal of GI endoscopists includes ERCP and endosonography. Endosonography is no longer a diagnostic procedure for the few where little harm is done but is widely practised with an increasing number of therapeutic possibilities. This makes EUS more complex. The therapeutic procedures have a particularly significant overlap with ERCP and demand a great deal of expertise. It seems that we have just touched the tip of the iceberg when it comes to simulation-based training for ERCP and EUS. This is in huge contrast with the fast developments in therapeutic indications and possibilities that these procedures offer. Models for ERCP training are already available but the full potential of these models have not yet been established, as well as their impact on clinical practice. Regarding EUS, data are even more scarce.

In a world where we are striving for more transparency in competency and procedural outcomes, simulation-based training is bound to have an increasingly important role. Certification and credentialing of simulator derived expertise would be the next logical step to ensure an optimal safety environment for everybody involved. The final stage of learning will always be to some extent patient-based. Our goal is that when this stage is reached we are dealing with trainees who have been well prepared by simulation-based scenarios.

Practice points

- The use of simulators in the early training setting accelerates the learning curve of basic endoscopy skills acquisition.
- Currently, both *ex vivo* and *in vivo* models provide the best platform to train advanced endoscopic procedures.
- There is no simulation-based training scenario available for common procedures like standard polypectomy.

Research agenda

- Development of a training platform for standard polypectomy and EMR of sessile polyps.
- Further development of simulation-based platforms for endosonography and ERCP and study of the transfer of simulator derived skills to patient-based endoscopy.
- Development of structured training programs with optimal use of simulator-based training.

Conflict of interest

None.

References

[1] Bini EJ, Firoozi B, Choung RJ, Ali EM, Osman M, Weinshel EH. Systematic evaluation of complications related to endoscopy in a training setting: a prospective 30-day outcomes study. Gastrointest Endosc 2003;57:8–16.
[2] Ekkelenkamp VE, Koch AD, de Man RA, Kuipers EJ. Training and competence assessment in GI endoscopy: a systematic review. Gut 2016;65(4):607–15.
[3] Carter FJ, Schijven MP, Aggarwal R, Grantcharov T, Francis NK, Hanna GB, et al. Consensus guidelines for validation of virtual reality surgical simulators. Surg Endosc 2005;19:1523–32.
[4] Gerson LB, Van Dam J. Technology review: the use of simulators for training in GI endoscopy. Gastrointest Endosc 2004; 60:992–1001.
[5] Carter FJ, Schijven MP, Aggarwal R, Grantcharov T, Francis NK, Hanna GB, et al. Consensus guidelines for validation of virtual reality surgical simulators. Simul Healthc 2006;1:171–9.
[6] Walsh CM, Sherlock ME, Ling SC, Carnahan H. Virtual reality simulation training for health professions trainees in gastrointestinal endoscopy. Cochrane Database Syst Rev 2012;6:CD008237.

[7] Moorthy K, Munz Y, Jiwanji M, Bann S, Chang A, Darzi A. Validity and reliability of a virtual reality upper gastrointestinal simulator and cross validation using structured assessment of individual performance with video playback. Surg Endosc 2004;18:328–33.
[8] Symbionix.
[9] Ruppin MCH. Practical training using a new gastrointestinal phantom. Endoscopy 1974;6:127–31.
[10] Hochberger J, Euler K, Naegel A, Hahn EG, Maiss J. The compact Erlangen active simulator for interventional endoscopy: a prospective comparison in structured team-training courses on 'endoscopic hemostasis' for doctors and nurses to the 'endo-trainer' model. Scand J Gastroenterol 2004;39:895–902.
[11] Giulio ED, Fregonese D, Casetti T, Cestari R, Chilovi F, D'Ambra G, et al. Training with a computer-based simulator achieves basic manual skills required for upper endoscopy: a randomized controlled trial. Gastrointest Endosc 2004;60:196–200.
[12] Ferlitsch A, Schoefl R, Puespoek A, Miehsler W, Schoeniger-Hekele M, Hofer H, et al. Effect of virtual endoscopy simulator training on performance of upper gastrointestinal endoscopy in patients: a randomized controlled trial. Endoscopy 2010;42:1049–56.
[13] Ende A, Zopf Y, Konturek P, Naegel A, Hahn EG, Matthes K, et al. Strategies for training in diagnostic upper endoscopy: a prospective, randomized trial. Gastrointest Endosc 2012;75:254–60.
[14] Ferlitsch A, Glauninger P, Gupper A, Schillinger M, Haefner M, Gangl A, et al. Evaluation of a virtual endoscopy simulator for training in gastrointestinal endoscopy. Endoscopy 2002;34:698–702.
[15] Sarker SK, Albrani T, Zaman A, Kumar I. Procedural performance in gastrointestinal endoscopy: live and simulated. World J Surg 2010;34:1764–70.
[16] Kim S, Spencer G, Makar GA, Ahmad NA, Jaffe DL, Ginsberg GG, et al. Lack of a discriminatory function for endoscopy skills on a computer-based simulator. Surg Endosc Interv Tech 2010;24:3008–15.
[17] McConnell R, Kim S, Ahmad NA, Falk GW, Forde KA, Ginsberg GG, et al. Lack of discriminatory function for endoscopy skills on a computer-based simulator. Gastrointest Endosc 2011;73:AB432.
[18] Shirai Y, Yoshida T, Shiraishi R, Okamoto T, Nakamura H, Harada T, et al. Prospective randomized study on the use of a computer-based endoscopic simulator for training in esophagogastroduodenoscopy. J Gastroenterol Hepatol 2008;23:1046–50.
[19] Qiao W, Bai Y, Lv R, Zhang W, Chen Y, Lei S, et al. The effect of virtual endoscopy simulator training on novices: a systematic review. PLoS ONE 2014;9.
[20] Plooy AM, Hill A, Horswill MS, Cresp ASG, Watson MO, Ooi SY, et al. Construct validation of a physical model colonoscopy simulator. Gastrointest Endosc 2012;76:144–50.
[21] Sedlack RE, Baron TH, Downing SM, Schwartz AJ. Validation of a colonoscopy simulation model for skills assessment. Am J Gastroenterol 2007;102:64–74.
[22] Fayez R, Feldman LS, Kaneva P, Fried GM. Testing the construct validity of the Simbionix GI Mentor II virtual reality colonoscopy simulator metrics: module matters. Surg Endosc Interv Tech 2010;24:1060–5.
[23] Felsher JJ, Olesevich M, Farres H, Rosen M, Fanning A, Dunkin BJ, et al. Validation of a flexible endoscopy simulator. Am J Surg 2005;189:497–500.
[24] Grantcharov TP, Carstensen L, Schulze S. Objective assessment of gastrointestinal endoscopy skills using a virtual reality simulator. JSLS 2005;9:130–3.
[25] Koch AD, Buzink SN, Heemskerk J, Botden SMBI, Veenendaal R, Jakimowicz JJ, et al. Expert and construct validity of the Simbionix GI Mentor II endoscopy simulator for colonoscopy. Surg Endosc Interv Tech 2008;22:158–62.
[26] Ritter EM, McClusky IDA, Lederman AB, Gallagher AG, Smith CD. Objective psychomotor skills assessment of experienced and novice flexible endoscopists with a virtual reality simulator. J Gastrointest Surg 2003;7:871–8.
[27] Haycock AV, Bassett P, Bladen J, Thomas-Gibson S. Validation of the second-generation Olympus colonoscopy simulator for skills assessment. Endoscopy 2009;41:952–8.
[28] Koch AD, Haringsma J, Schoon EJ, de Man RA, Kuipers EJ. A second-generation virtual reality simulator for colonoscopy: validation and initial experience. Endoscopy 2008;40:735–8.
[29] Sugden C, Aggarwal R, Banerjee A, Haycock A, Thomas-Gibson S, Williams CB, et al. The development of a virtual reality training curriculum for colonoscopy. Ann Surg 2012;256:188–92.
[30] Datta V, Mandalia M, Mackay S, Darzi A. The PreOp flexible sigmoidoscopy trainer: validation and early evaluation of a virtual reality based system. Surg Endosc 2002;16:1459–63.
[31] MacDonald J, Ketchum J, Williams RG, Rogers LQ. A lay person vs a trained endoscopist: can the preop endoscopy simulator detect a difference? Surg Endosc Interv Tech 2003;17:896–8.
[32] Mahmood T, Darzi A. A study to validate the colonoscopy simulator: it is usefully discriminatory for more than one measurable outcome. Surg Endosc 2003;17:1583–9.
[33] Tuggy ML. Virtual reality flexible sigmoidoscopy simulator training: impact on resident performance. J Am Board Fam Pract 1998;11:426–33.
[34] Ahad S, Boehler M, Schwind CJ, Hassan I. The effect of model fidelity on colonoscopic skills acquisition. A randomized controlled study. J Surg Educ 2013;70:522–7.
[35] Ahlberg G, Hultcrantz R, Jaramillo E, Lindblom A, Arvidsson D. Virtual reality colonoscopy simulation: a compulsory practice for the future colonoscopist? Endoscopy 2005;37:1198–204.
[36] Kruglikova I, Grantcharov TP, Drewes AM, Funch-Jensen P. The impact of constructive feedback on training in gastrointestinal endoscopy using high-fidelity virtual-reality simulation: a randomised controlled trial. Gut 2010;59:181–5.
[37] Mahmood T, Darzi A. The learning curve for a colonoscopy simulator in the absence of any feedback: No feedback, no learning. Surg Endosc 2004;18:1224–30.
[38] Sedlack RE, Kolars JC, Alexander JA. Computer simulation training enhances patient comfort during endoscopy. Clin Gastroenterol Hepatol 2004;2:348–52.
[39] Snyder CW, Vandromme MJ, Tyra SL, Hawn MT. Retention of colonoscopy skills after virtual reality simulator training by independent and proctored methods. Am Surg 2010;76:743–6.
[40] Park J, MacRae H, Musselman LJ, Rossos P, Hamstra SJ, Wolman S, et al. Randomized controlled trial of virtual reality simulator training: transfer to live patients. Am J Surg 2007;194:205–11.

[41] Van Sickle KR, Buck L, Willis R, Mangram A, Truitt MS, Shabahang M, et al. A multicenter, simulation-based skills training collaborative using shared GI mentor II systems: results from the Texas association of surgical skills laboratories (TASSL) flexible endoscopy curriculum. Surg Endosc Interv Tech 2011;25:2980–6.

[42] Haycock A, Koch AD, Familiari P, van Delft F, Dekker E, Petruzziello L, et al. Training and transfer of colonoscopy skills: a multinational, randomized, blinded, controlled trial of simulator versus bedside training. Gastrointest Endosc 2010;71:298–307.

[43] G W. The world of civil simulators. Flight Int Mag 1978;435.

[44] Frimberger E, von Delius S, Rösch T, Karagianni A, Schmid RM, Prinz C. A novel and practicable ERCP training system with simulated fluoroscopy. Endoscopy 2008;40:517–20.

[45] Leung JW, Lee JG, Rojany M, Wilson R, Leung FW. Development of a novel ERCP mechanical simulator. Gastrointest Endosc 2007;65:1056–62.

[46] von Delius S, Thies P, Meining A, Wagenpfeil S, Burian M, Huber W, et al. Validation of the X-vision ERCP training system and technical challenges during early training of sphincterotomy. Clin Gastroenterol Hepatol 2009;7:389–96.

[47] Lim BS, Leung JW, Lee J, Yen D, Beckett L, Tancredi D, et al. Effect of ERCP mechanical simulator (EMS) practice on trainees ERCP performance in the early learning period: US multicenter randomized controlled trial. Am J Gastroenterol 2011;106:300–6.

[48] Liao WC, Leung J, Wang HP, Chang WH, Chu CH, Lin JT, et al. Coached practice using ERCP mechanical simulator improves trainees' ERCP performance: a randomized controlled trial. Endoscopy 2013;45:799–805.

[49] Sedlack RE, Petersen BT, Kolars JC. The impact of a hands-on ERCP workshop on clinical practice. Gastrointest Endosc 2005;61:67–71.

[50] Parra-Blanco A, Gonzalez N, Gonzalez R, Ortiz-Fernandez-Sordo J, Ordieres C. Animal models for endoscopic training: do we really need them? Endoscopy 2013;45:478–84.

[51] Neumann M, Mayer G, Ell C, Felzmann T, Reingruber B, Horbach T, et al. The Erlangen endo-trainer: life-like simulation for diagnostic and interventional endoscopic retrograde cholangiography. Endoscopy 2000;32:906–10.

[52] Sedlack R, Petersen B, Binmoeller K, Kolars J. A direct comparison of ERCP teaching models. Gastrointest Endosc 2003;57:886–90.

[53] Bittner IJG, Mellinger JD, Imam T, Schade RR, MacFadyen Jr BV. Face and construct validity of a computer-based virtual reality simulator for ERCP. Gastrointest Endosc 2010;71:357–64.

[54] Sahakian AB, Laine L, Jamidar PA, Siddiqui UD, Duffy A, Ciarleglio MM, et al. Can a computerized simulator assess skill level and improvement in performance of ERCP? Dig Dis Sci. 2016 Mar;61(3):722–30.

[55] Grimm H, Binmoeller KF, Soehendra N. Endosonography-guided drainage of a pancreatic pseudocyst. Gastrointest Endosc 1992;38:170–1.

[56] Barthet M, Gasmi M, Boustiere C, Giovannini M, Grimaud JC, Berdah S, et al. EUS training in a live pig model: does it improve echo endoscope hands-on and trainee competence? Endoscopy 2007;39:535–9.

[57] Haycock AV, Youd P, Bassett P, Saunders BP, Tekkis P, Thomas-Gibson S. Simulator training improves practical skills in therapeutic GI endoscopy: results from a randomized, blinded, controlled study. Gastrointest Endosc 2009;70:835–45. e2.

[58] Committee AT, Hwang JH, Konda V, Abu Dayyeh BK, Chauhan SS, Enestvedt BK, et al. Endoscopic mucosal resection. Gastrointest Endosc 2015;82:215–26.

[59] Terasaki M, Tanaka S, Oka S, Nakadoi K, Takata S, Kanao H, et al. Clinical outcomes of endoscopic submucosal dissection and endoscopic mucosal resection for laterally spreading tumors larger than 20 mm. J Gastroenterol Hepatol 2012;27:734–40.

[60] Toyokawa T, Inaba T, Omote S, Okamoto A, Miyasaka R, Watanabe K, et al. Risk factors for perforation and delayed bleeding associated with endoscopic submucosal dissection for early gastric neoplasms: analysis of 1123 lesions. J Gastroenterol Hepatol 2012;27:907–12.

[61] Probst A, Golger D, Anthuber M, Markl B, Messmann H. Endoscopic submucosal dissection in large sessile lesions of the rectosigmoid: learning curve in a European center. Endoscopy 2012;44:660–7.

[62] Oda I, Odagaki T, Suzuki H, Nonaka S, Yoshinaga S. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc 2012;24(Suppl. 1):129–32.

[63] Chiu PW, Teoh AY, To KF, Wong SK, Liu SY, Lam CC, et al. Endoscopic submucosal dissection (ESD) compared with gastrectomy for treatment of early gastric neoplasia: a retrospective cohort study. Surg Endosc 2012;26:3584–91.

[64] Coman RM, Gotoda T, Draganov PV. Training in endoscopic submucosal dissection. World J Gastrointest Endosc 2013;5:369–78.

[65] 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.

[66] Kakushima N, Fujishiro M, Kodashima S, Muraki Y, Tateishi A, Omata M. A learning curve for endoscopic submucosal dissection of gastric epithelial neoplasms. Endoscopy 2006;38:991–5.

[67] 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.

[68] Yamamoto S, Uedo N, Ishihara R, Kajimoto N, Ogiyama H, Fukushima Y, et al. Endoscopic submucosal dissection for early gastric cancer performed by supervised residents: assessment of feasibility and learning curve. Endoscopy 2009;41:923–8.

[69] Hochberger J, Maiss J, Magdeburg B, Cohen J, Hahn EG. Training simulators and education in gastrointestinal endoscopy: current status and perspectives in 2001. Endoscopy 2001;33:541–9.

[70] 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.

[71] Parra-Blanco A, Arnau MR, Nicolas-Perez D, Gimeno-Garcia AZ, Gonzalez N, Diaz-Acosta JA, et al. Endoscopic submucosal dissection training with pig models in a Western country. World J Gastroenterol 2010;16:2895–900.

[72] Vazquez-Sequeiros E, de Miquel DB, Olcina JR, Martin JA, Garcia M, Lucas DJ, et al. Training model for teaching endoscopic submucosal dissection of gastric tumors. Rev Esp Enferm Dig 2009;101:546–52.

[73] Martinek J, Stefanova M, Suchanek S, Zavada F, Svobodova B, Strosova A, et al. Training of different endoscopic skills on ex-vivo animal model. Simul Healthc 2014;9:112–9.

[74] Herreros de Tejada A. ESD training: a challenging path to excellence. World J Gastrointest Endosc 2014;6:112–20.
[75] Yoshida N, Yagi N, Inada Y, Kugai M, Kamada K, Katada K, et al. Possibility of ex vivo animal training model for colorectal endoscopic submucosal dissection. Int J Colorectal Dis 2013;28:49–56.
[76] Tanaka S, Morita Y, Fujita T, Wakahara C, Ikeda A, Toyonaga T, et al. Ex vivo pig training model for esophageal endoscopic submucosal dissection (ESD) for endoscopists with experience in gastric ESD. Surg Endosc 2012;26:1579–86.
[77] Kato M, Gromski M, Jung Y, Chuttani R, Matthes K. The learning curve for endoscopic submucosal dissection in an established experimental setting. Surg Endosc 2013;27:154–61.
[78] Hon SS, Ng SS, Lee JF, Li JC, Lo AW. In vitro porcine training model for colonic endoscopic submucosal dissection: an inexpensive and safe way to acquire a complex endoscopic technique. Surg Endosc 2010;24:2439–43.
[79] Pioche M, Rivory J, Aguero-Garcete G, Guillaud O, O'Brien M, Lafon C, et al. New isolated bovine colon model dedicated to colonic ESD hands-on training: development and first evaluation. Surg Endosc 2015;29:3209–15.
[80] Hochberger J, Neumann M, Hohenberger W, Hahn EG. Neuer Endoskopie-Trainer für die therapeutische flexible Endoskopie. Z Gastroenterol 1997;35:722–3.
[81] Bok GH, Cho JY. ESD hands-on course using ex vivo and in vivo models in South Korea. Clin Endosc 2012;45:358–61.
[82] Shi Q, Zhong YS, Yao LQ, Zhou PH, Xu MD, Wang P. Endoscopic submucosal dissection for treatment of esophageal submucosal tumors originating from the muscularis propria layer. Gastrointest Endosc 2011;74:1194–200.
[83] Horii J, Goto O, Shimoda M, Sasaki M, Fujimoto A, Ochiai Y, et al. Which part of a porcine stomach is suitable as an animal training model for gastric endoscopic submucosal dissection? Endoscopy 2016;48:188–93.
[84] Coda S, Trentino P, Antonellis F, Porowska B, Gossetti F, Ruberto F, et al. A western single-center experience with endoscopic submucosal dissection for early gastrointestinal cancers. Gastric Cancer 2010;13:258–63.
[85] 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.
[86] Uraoka T, Parra-Blanco A, Yahagi N. Colorectal endoscopic submucosal dissection: is it suitable in western countries? J Gastroenterol Hepatol 2013;28:406–14.

VI. ANIMAL MODEL SIMULATION FOR ADVANCED ENDOSCOPIC RESECTION TECHNIQUES

A) VALIDATION OF THE MODEL

TRAINING IN ENDOSCOPIC MUCOSAL RESECTION AND ENDOSCOPIC SUBMUCOSAL DISSECTION: FACE, CONTENT AND EXPERT VALIDITY OF THE LIVE PORCINE MODEL.

Küttner-Magalhães R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD.

United European Gastroenterol J. 2018;6(4):547-557. doi: 10.1177/2050640617742484.

UNITED EUROPEAN GASTROENTEROLOGY ueg journal

Original Article

United European Gastroenterology Journal
2018, Vol. 6(4) 547–557

Reprints and permissions:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/2050640617742484
journals.sagepub.com/home/ueg
SAGE

Training in endoscopic mucosal resection and endoscopic submucosal dissection: Face, content and expert validity of the live porcine model

Ricardo Küttner-Magalhães[1], Mário Dinis-Ribeiro[2,3], Marco J Bruno[4], Ricardo Marcos-Pinto[1,3,5], Carla Rolanda[6,7,8] and Arjun D Koch[4]

Abstract

Introduction: Endoscopic mucosal resection and endoscopic submucosal dissection are demanding procedures. This study aims to establish face, content and expert validity of the live porcine model in performing endoscopic mucosal resection, endoscopic submucosal dissection, complication management and to assess it as a training tool.

Material and methods: Tutors and trainees participating in live porcine model endoscopic mucosal resection and endoscopic submucosal dissection workshops filled out a questionnaire regarding the realism of the model compared to human setting and its role as a learning tool. A 10-point Likert scale was used.

Results: Ninety-one endoscopists (13 tutors; 78 trainees) were involved in four workshops. Median global classifications for the realism of the life porcine model ranged between 7.0–8.0 (interquartile range 5.0–9.0). Procedures resembled human cases with a median of 9.0 (8.0–9.0) for oesophageal multiband endoscopic mucosal resection; 8.5 (8.0–9.0) for oesophageal endoscopic submucosal dissection; 9.0 (8.0–10.0) for gastric endoscopic submucosal dissection; and 9.0 (8.5–9.75 and 8.0–9.69) for complication detection and management. The animal model as a learning tool had median scores of 9.0 (7.0–10.0) considering how procedures are performed; 9.0–9.5 (8.0–10.0) for usefulness for beginners; and 9.0–10.0 (5.0–10.0) regarding it a prerequisite.

Conclusions: Training in a live porcine model was considered very realistic compared to the human setting and was highly appreciated as a learning tool. This is the first study to establish face, content and expert validity of the live porcine model in performing multiband endoscopic mucosal resection, oesophageal and gastric endoscopic submucosal dissection. The validation of this model provides the rationale to incorporate it into formal teaching programmes.

Keywords

Training in endoscopy, simulation in endoscopy, live porcine model, endoscopic mucosal resection, endoscopic submucosal dissection

Received: 8 August 2017; accepted: 17 October 2017

[1]Department of Gastroenterology, Santo António Hospital, Porto Hospital Centre, Portugal
[2]Department of Gastroenterology, Oncology Portuguese Institute of Porto, Porto, Portugal
[3]Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS) and Center for Research in Health Technologies and Services (CINTESIS), Faculty of Medicine of Porto, Porto, Portugal
[4]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[5]Abel Salazar Institute of Biomedical Sciences, University of Porto, Porto, Portugal
[6]Department of Gastroenterology, Braga Hospital, Braga, Portugal
[7]Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal
[8]ICVS/3B's, PT Government Associate Laboratory, Braga, Portugal

Corresponding author:
Ricardo Küttner-Magalhães, Department of Gastroenterology, Santo António Hospital, Porto Hospital Centre, Largo Prof. Abel Salazar 4099-001, Porto, Portugal.
Email: rkuttner@gmail.com

Key summary

1. Summarise the established knowledge on this subject

- EMR and ESD are demanding procedures requiring extensive training.
- Numerous live animal courses are organised throughout the world and, until now, a scientific basis in the form of a formal validation of this model has been lacking.

2. What are the significant and/or new findings of this study?

- This study provides face, content and expert validity of the live porcine model in performing EMR, ESD and complication management.
- This validation adds to the ethical justification of animal sacrifice for medical training purposes and provides the rationale to incorporate it into formal teaching programmes.
- This validation may have an impact on the justification to apply for funding and may form the basis for future studies.

Introduction

Complex advanced endoscopic procedures, such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are considered treatment options for pre-malignant and early neoplastic lesions. These challenging procedures require practical skills obtained through extensive training, are time-consuming and have the potential for serious adverse events.[1–3]

Multiband mucosectomy (MBM) is one of the EMR techniques that uses a multiband ligation kit enabling sequential banding and snare resection without removing the endoscope, facilitating resections of extensive superficial lesions. It has been used mainly in the oesophagus for the treatment of Barrett's early cancer.[4,5]

ESD was developed in Japan in the mid-1990s and has expanded gradually to other countries ever since. The major advantages of this technique are the ability to achieve en-bloc resections allowing for an accurate tumour histopathological staging and grading with precise evaluation of resection margins, R0 resections and lower rates of local recurrence.[2,6,7]

A learning curve in the performance of ESD has been demonstrated, and more experienced endoscopists have a higher rate of en-bloc resection, reduced procedure duration and fewer related adverse events.[8,9]

In the East, ESD teaching has followed the traditional master-apprentice model with hands-on human cases supervised by expert endoscopists.[9,10] However in Western countries the number of highly qualified ESD experts is low and the prevalence of gastric superficial neoplasms is much lower, diminishing the opportunity to start performing ESD on the easiest and safest locations. Therefore, in Western countries, a pre-patient training programme, including simulation models, is recommended.[2,11–13]

Currently, existing training programmes have consistently included: acquiring basic knowledge, practicing on animal models (ex vivo animal organs and live porcine models), visiting centres with a high ESD volume, attendance of hands-on training ESD workshops and only then proceeding to clinical practice, ideally under supervision by an expert when available during the first cases.[2,11–13]

Workshops using animal models are being organised in many specialised training centres with the potential to aid in speeding up the learning process and achieving initial competence in ESD in a safe learning environment with direct one-on-one expert supervision.[14–16]

It seems logical to practise skills in advanced endoscopic resections in a live porcine model, which is considered to have the closest resemblance to the human anatomy.

However, for every technology, teaching tool or method, and particularly in the case of a live animal model, evidence to support its validity should first be established before its wide practice use, sacrifice of animals and financial resources employment.

The validation process should start from basic premises and, accordingly, it is necessary to prove the live porcine model provides a realistic comparison to the real-life human setting. Validity of the model can be established by studying face, content and expert validity.

Face validity refers to the degree to which a model appears to represent the intended purpose as assessed by its users. Content validity refers to the extent to which the content of the model incorporates all the relevant, appropriate, comprehensive and consistent domains of items that we want to assess. Expert validity is attained when this appreciation is recognised by experts in the field.[17–19]

This study aims to establish face, content and expert validity of the live porcine model in performing ESD and EMR and subsequent complication management, in order to assess its value as a training tool.

Material and methods

Study design

Animal model. Live pigs (*Sus scrofus domesticus*) weighing between 30–40 kg were used. The animals were given a liquid diet for three days and fasted for eight hours before the procedures. With the support of the veterinarian staff throughout the course, general anaesthesia with endotracheal intubation and mechanical ventilation was performed according to local protocol.

Participants. Faculty members (tutors) and trainees attending a course for EMR/ESD training using live porcine were invited to fill out a questionnaire at the end of the two-day workshop they were involved.

Validation questionnaire. The questionnaire contains 75 questions in three separate domains. This questionnaire is based on similar validation questionnaires from previous studies from our group.[20,21] The first part is related to demographic data and includes level and range of endoscopic and simulators experience. The second part is centred on the realism of the animal model, namely in accomplishing multiband EMR, ESD and dealing with complications, compared to human setting. The final part is focused on the animal model as a learning tool. Appreciation is reported in a 10-point Likert scale. The complete questionnaire is available in Appendix 1.

Simulation. Each workshop had a duration of two days and took place in the training centres of the Erasmus School of Endoscopy at the Erasmus University Medical Center in Rotterdam, the Netherlands and the School of Health Sciences, University of Minho (ECS-UM) in Braga, Portugal.

Six fully equipped interventional endoscopy workstations were used under the guidance of international faculty experts (Figure 1). Storz and Pentax flexible endoscopes were used. The electrosurgical units were the ERBE VIO 200s. The training modules consisted of EMR in the oesophagus using the Duette multiband mucosectomy kit (Cook Ireland Ltd, Limerick, Ireland) and ESD in oesophagus and stomach using ERBE Hybrid Knives (ERBE, Tübingen, Germany). During both EMR and ESD, trainees were instructed to mark the outer margins of a pseudo-lesion. EMR was carried out using multiband mucosectomy, where band ligation was applied followed by snare resection of the created pseudo-polyp and inspection of the ulcer. ESD was executed by performing submucosal injection and creating a circumferential incision, followed by submucosal dissection and re-lifting the pseudo-lesion when needed (Figure 2). Any complication such as bleeding or perforation was subsequently managed by the trainees as an integral part of the training course, using injection, coagulation with bipolar haemostatic forceps (HemoStat-Y; Pentax, Tokyo, Japan) and clip application (Instinct clip; Cook Medical, Winston-Salem, North Carolina, USA).

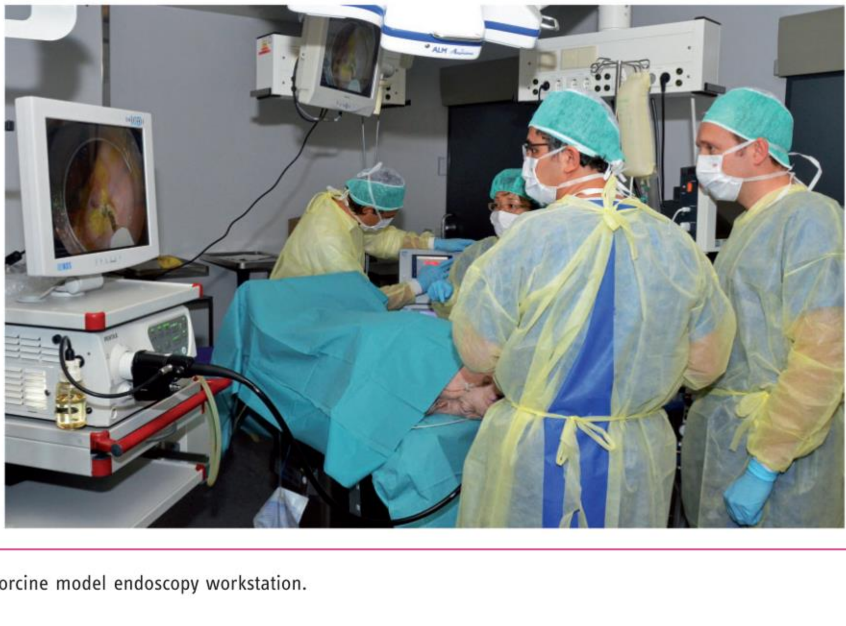

Figure 1. Live porcine model endoscopy workstation.

Figure 2. Performance of endoscopic submucosal dissection on porcine model.

Statistical analysis

Descriptive statistics were determined for all measures according to type of variables. Proportions were reported for dichotomous and ordinal variables. For continuous variables the mean (as a more intuitive measure) and median (interquartile range (IQR) 25–75%) were described. Non-parametric tests were used to assess statistical differences.

The IBM Statistical Package for Social Sciences (SPSS Version 23.0.0; SPSS Inc., Chicago, Illinois, USA) was used to manage data.

Results

Participants

A total of 91 endoscopists (13 tutors and 78 trainees) were involved in four live porcine model workshops organised in 2014 and 2015. Background characteristics, previous endoscopic and courses experience for each group are summarised in Table 1. All the tutors, as well as the majority of the trainees were fully trained gastroenterologists, working in academic or tertiary hospitals. General endoscopic experience of participants was higher for tutors, particularly for more complex procedures, as was the previous participation in simulator courses.

Realism of the live porcine model

The median global classifications of the items related to the realism of the life porcine model, ranged between 8.0 and 7.0 (IQR 5.0–9.0) (Table 2). Overall appearance reached the highest mean global classification of 8.2, whereas wall structure of organ and mucosal thickness attained the lowest value of 6.9 and 6.3, respectively.

Realism of procedures

Procedures were globally considered to closely resemble human cases, for oesophageal multiband EMR with a median of 9.0 (IQR 8.0–9.0), for oesophageal ESD with a median of 8.5 (IQR 8.0–9.0), for gastric ESD with a median of 9.0 (IQR 8.0–10.0) and for complication detection and management with a median of 9.0 (IQR 8.5–9.75 and 8.0–9.69, respectively) (Table 3). In general, trainee's scores were equal or slightly higher than those of the tutors.

The animal model as a learning tool

Median ratings regarding understanding how procedures are performed and coordination of tasks were 9.0 (IQR 7.0–10.0) for all the items evaluated. Global means were lowest for oesophageal ESD (8.3) and higher for gastric ESD (8.9) (Table 4).

Procedure difficulty had a median of 8.0 (IQR 4.0–9.0), whereas the lowest mean value was on oesophageal ESD (6.7) and the highest on complication detection and management (8.1).

Live animal simulated oesophageal EMR, oesophageal ESD and gastric ESD were considered highly useful for beginners with median global values ranging from 9.0 to 9.5 (8.0–10.0).

Participants considered that live animal courses should be a prerequisite before clinical practice (median global values of 9.0 (IQR 5.0–10.0) for oesophageal EMR and 10.0 (IQR 9.0–10,0) for oesophageal and gastric ESD).

Trainees considered the usefulness of life animal simulated procedures and the necessity of courses with live animal models to be a prerequisite before clinical practice with higher scores than tutors for oesophageal and gastric ESD.

Discussion

To our knowledge this is the first study to formally address the face, expert and content validity of the live porcine model in training for EMR and ESD. Our results demonstrate that the model is very realistic and that procedures accurately resemble human cases. Moreover, the simulation process is highly appreciated as a learning tool by both tutors and trainees alike. In our opinion the results of this study justify the application of the live porcine model to formally train endoscopists in performing EMR and ESD and complication management before proceeding to human cases.

Simulators allow a novice or expert to perform a new technique or use a new accessory thereby avoiding putting human patients to the potential risks associated with the initial, steepest part of the learning curve.[22]

Table 1. Background characteristics, endoscopic and courses experience of participants.

	Tutor (*n* = 13) *n* (%)	Trainee (*n* = 78) *n* (%)
Background characteristics		
Median age (range)	42 (34–43)	38 (27–67)
Gastroenterologists	13 (100)	65 (83)
Surgeons	–	9 (12)
Academic or tertiary hospital	13 (100)	46 (59)
Fully trained physicians	13 (100)	48 (62)
Trainee physicians	–	16 (21)
Previous endoscopic experience		
Colonoscopies:≥201/year;≥601 total	13 (100); 13 (100)	63 (81); 65 (83)
Upper endoscopies:≥201/year;≥601 total	12 (92); 13 (100)	70 (90); 71 (91)
ERCP:≥101/year;≥201 total	6 (46); 8 (62)	20 (26); 32 (41)
EUS:≥101/year;≥201 total	6 (46); 8 (62)	14 (18); 19 (24)
Oesophageal EMR:≥1/year;≥21 total	12 (92); 11(85)	38 (49); 13 (17)
Gastric EMR:≥1/year;≥21 total	13 (100); 12 (92)	48 (62); 18 (23)
Colonic EMR:≥1/year;≥21 total	13 (100); 13 (100)	59 (76); 48 (62)
Colonic EMR:≥21/year;≥51 total	13 (100); 13 (100)	34 (44); 35 (45)
EMR: inject and snare technique	13 (100)	71 (91)
EMR: band and snare technique	12 (92)	43 (55)
EMR: cap and snare technique	12 (92)	36 (46)
ESD:≥1/year;≥21 ESD total	12 (92); 12 (92)	11 (14); 4 (5)
Previous course experience		
Computerised/virtual-reality simulators	4 (31)	21 (27)
Explanted (ex vivo) animal models	8 (62)	33 (42)
Live animal models	12 (92)	41 (53)

EMR: endoscopic mucosal resection; ERCP: endoscopic retrograde cholangiopancreatography; ESD: endoscopic submucosal dissection; EUS: endoscopic ultrasonography.

Pure mechanical simulators and virtual reality (VR) simulators are not ideal when addressing advanced endoscopic resection training, due to the inability to reproduce the elasticity, tissue properties and tactile feedback of human tissue.[23] This study demonstrates that the live porcine model received high ratings on these items, supporting its value and use for this training.

Trainees in our study were already experienced in performing endoscopic procedures such as upper endoscopy and colonoscopy (and to a lesser extent endoscopic retrograde cholangiopancreatography (ERCP) and EUS: endoscopic ultrasonography (EUS)). The majority had previous experience in EMR, mostly in the colon and used several EMR techniques. For that reason they seem well fitted to assess the realism of the porcine training model for EMR and ESD. The fact that appreciation by the trainees was similar to the ones given by the experts supports this view even more. It shows that both experts and trainees are highly capable of assessing the validity of this training model and strengthens the robustness of the data presented.

Regarding the live animal model, orientation of organs, thickness and stiffness of the mucosal layer have been considered distinct from the human scenario.[24,25] Accordingly, in our study, wall structure of organ, mucosal thickness and tissue pliability scored the lowest mean values, although medians were comparable. This seems in line with the study by Horii et al. where mucosal layer of the porcine was found to be thinner in the proximal stomach and thicker in the distal area, particularly at the level of the greater curvature, where ESD speed is lower and difficulty is greater when compared to human procedures. It has been suggested that the greater curvature, particularly the distal part of the porcine stomach is the least suitable place for ESD training.[26]

The ability to apply band ligation and to cut the created pseudopolyp, while performing oesophageal

Table 2. Realism of the live porcine.

	Tutor ($n = 13$) Mean Median (IQR)	Trainee ($n = 78$) Mean Median (IQR)	Global ($n = 91$) Mean Median (IQR)
Overall appearance	7.5 8.0 (7.0–8.0)	8.3 8.0 (8.0–9.0)	8.2 8.0 (7.0–9.0)
Overall difficulty	7.5 8.0 (7.0–8.5)	8.1 8.0 (7.2–9.0)	8.1 8.0 (7.0–9.0)
Anatomy	7.2 7.0 (7.0–8.0)	7.9 8.0 (7.0–9.0)	7.8 8.0 (7.0–9.0)
Size of organ	7.2 7.0 (6.5–8.0)	7.8 8.0 (7.0–9.0)	7.7 8.0 (7.0–9.0)
Wall structure of organ	7.1 7.0 (6.0–8.0)	6.9 7.0 (6.0–8.0)	6.9 7.0 (6.0–8.0)
Mucosal thickness	6.0 7.0 (5.0–7.0)	6.4 6.5 (5.0–8.0)	6.3 7.0 (5.0–8.0)
Tissue pliability/ elasticity	7.1 7.0 (7.0–8.0)	7.0 7.0 (6.0–8.0)	7.0 7.0 (6.0–8.0)
Tactile feedback	7.2 7.0 (6.5–8.0)	7.7 8.0 (7.0–9.0)	7.6 8.0 (7.0–9.0)

IQR: interquartile range.
Results are presented as mean and median (IQR 25–75%); Mann-Whitney test used as non-parametric test.

multiband mucosectomy, was rated slightly lower compared to the other steps in this technique. We feel that this is related to a subjective impression that, due to the difference in wall structure compared to human oesophagus, suction of the pseudolesion is different. Unlike in human practice, it is relatively easy to create a pseudopolyp containing a full thickness specimen resulting more often in a perforation. The aforementioned difference in the porcine oesophagus also explains why oesophageal ESD had lower overall scores.

In addition to the high scores on issues related to the realism of the live porcine model, the performance of the procedures itself was considered very similar to the human practice, as well. Moreover, the difficulty of procedures and usefulness of life animal simulated procedures had high ratings. We think that this is related to the fact that animal models, such as intubated, anaesthetised pigs, have breathing movements, heart beats, peristalsis, intraluminal secretions, tissue reaction to injection and electrocautery, and abdominal distension which makes the model approach the human setting. The same properties make it possible to deal with adverse events, such as bleeding and perforation.[11,15,25,27]

When teaching ESD, the process of submucosal dissection has been considered the most challenging one and its difficulty is related mainly to controlling haemorrhage.[28] We found that ratings addressing the porcine model on complication detection and management, namely controlling haemorrhage, were very high, emphasising the value of the model in training all the steps involved in ESD. Our study clearly demonstrates that the live porcine model is not only a valid model for training EMR and ESD procedures, but also for training of intraprocedural complication management.

It has been suggested that ex vivo models cannot substitute for in vivo training to acquire competence in ESD and some advocate only moving to the live animal model after acquiring basic ESD skills using explanted organs.[16,27,29] Nonetheless, issues pertaining ethics, dedicated facilities, equipment, veterinarian support, availability of general anaesthesia and preparation of the animal, including intensive bowel cleansing (in the case of colorectal ESD), euthanasia or follow-up care (when performing survival studies), as well as financial considerations may limit its use.[11,15,25,27,30] Animal models have been incorporated in ESD training programmes by different groups. Although previous papers have focused on feasibility of ESD, validation of the model itself has not been formally demonstrated. Considering the evidence gathered in this study, including the validation of the live porcine model in training EMR and ESD, we believe that live pig workshops should be formally incorporated in teaching programmes. This fact may have an impact on the justification to apply for funding. Similarly, the current scientific substantiation of a live pig model to train for EMR and ESD, adds to the ethical justification of animal sacrifice for such medical training purposes.

This article may serve as a framework for future studies on subjects such as learning curves and how to get the most out of animal training before proceeding to human cases.

With regard to the strengths of our study, we underline its relevance, the multicentre character of the hosting labs and the origin of tutors and trainees which, in turn, serves as an argument for the generalization of the achieved results.

Concerning limitations of our study, we stress that the porcine colon was not evaluated. Also, procedures were conducted on healthy porcine tissues without pathologic conditions, unlike the real human scenario where genuine mucosal/submucosal lesions are being treated and in which, for example, fibrosis may be an issue. Nevertheless this limitation is probably of reduced magnitude given that in a great number of patients these features will not alter the procedure and that novices in ESD, for whom this training is most valuable, should not start ESD in difficult, large and fibrotic lesions.

Table 3. Procedures in the live porcine model.

Procedure	Tutor ($n=13$) Mean Median (IQR)	Trainee ($n=78$) Mean Median (IQR)	Global ($n=91$) Mean Median (IQR)
Overall experience with multiband EMR	8.1 8.0 (8.0–9.0)	8.3 9.0 (7.25–10.0)	8.3 9.0 (8.0–9.0)
Oesophageal multiband EMR			
Ability to inspect the oesophagus	8.1 8.0 (7.5–9.0)	8.5 9.0 (7.0–10.0)	8.4 9.0 (7.0–9.0)
Ability to mark the outer margins of pseudolesion	8.2 8.0 /7.3–9.0)	8.6 9.0 (8.0–10.0)	8.5 9.0 (8.0–10.0)
Ability to apply band ligation	8.1 8.0 (7.0–9.0)	7.8 8.0 (7.0–9.0)	7.8 8.0 (7.0–9.0)
Ability to cut the created pseudopolyp	8.1 8.0 (7.5–9.0)	7.9 8.5 (7.0–9.0)	7.9 8.0 (7.0–9.0)
Ability to inspect the ulcer	8.2 8.0 (7.5–9.0)	8.4 9.0 (8.0–10.0)	8.3 8.5 (8.0–10.0)
Overall oesophageal ESD experience	8.3 8.25 (8.0–9.0)	8.1 8.75 (8.0–9.5)	8.2 8.5 (8.0–9.0)
Oesophageal ESD			
Ability to inspect the oesophagus	8.5 8.0 (8.0–9.0)	8.2 9.0 (8.0–9.5)	8.2 8.0 (8.0–9.0)
Ability to mark the outer margins of pseudolesion	8.6 8.5 (8.0–9.0)	8.3 9.0 (7.0–10.0)	8.4 9.0 (8.0–9.0)
Ability to inject and perform circumferential incision	8.0 8.0 (7.8–9.0)	7.8 8.0 (6.0–9.0)	7.9 8.0 (7.0–9.0)
Ability to inject to lift the pseudolesion	8.2 8.0 (7.8–9.0)	8.0 8.0 (7.0–9.3)	8.0 8.0 (7.3–9.0)
Ability to perform submucosal dissection	8.0 8.0 (8.0–9.0)	7.9 8.0 (7.0–9.0)	7.9 8.0 (8.0–9.0)
Ability to inspect the ulcer	8.6 8.5 (8.0–9.0)	8.4 9.0 (8.0–10.0)	8.4 9.0 (8.0–9.8)
Overall gastric ESD experience	8.3 8.5 (7.88–9.0)	8.8 9.0 (8.0–10.0)	8.7 9.0 (8.0–10.0)
Gastric ESD			
Ability to inspect the stomach	7.9 8.0 (7.3–8.8)	8.7 9.0 (8.0–10.0)	8.6 9.0 (8.0–10.0)
Ability to mark the outer margins of pseudolesion	8.5 8.5 (8.0–9.0)	9.0 9.0 (8.0–10.0)	8.9 9.0 (8.0–10.0)
Ability to inject and perform circumferential incision	7.4 7.5 (7.0–9.0)	8.4 8.0 (8.0–10.0)	8.2 8.0 (7.0–9.3)
Ability to inject to lift the pseudolesion	7.8 8.5 (7.0–9.0)	8.4 8.0 (8.0–9.3)	8.3 8.0 (8.0–9.0)
Ability to perform submucosal dissection	8.3 8.5 (8.0–9.0)	8.5 9.0 (8.0–10.0)	8.5 9.0 (8.0–9.0)
Ability to inspect the ulcer	8.7 9.0 (8.0–9.0)	9.0 9.0 (8.0–10.0)	8.9 9.0 (8.0–10.0)
Overall complication detection	8.8 8.88 (8.38–9.0)	9.1 9.25 (8.5–9.69)	9.0 9.0 (8.5–9.75)

(continued)

Table 3. Continued

Procedure	Tutor ($n=13$) Mean Median (IQR)	Trainee ($n=78$) Mean Median (IQR)	Global ($n=91$) Mean Median (IQR)
Ability to detect bleeding	8.7	9.0	8.9
	9.0 (8.0–9.0)	9.0 (8.5–10.0)	9.0 (8.0–10.0)
In the oesophagus	8.8	9.0	8.9
	9.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
In the stomach	8.6	8.9	8.9
	9.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
Ability to detect perforations	9.0	9.0	9.0
	9.0 (8.38–9.0)	9.0 (8.13–10.0)	9.0 (8.0–10.0)
In the oesophagus	9.1	9.1	9.1
	9.0 (9.0–9.8)	9.0 (8.0–10.0)	9.0 (8.8–10.0)
In the stomach	8.8	9.0	8.9
	9.0 (8.3–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
Overall complication management	8.5	8.8	8.8
	8.25 (8.0–8.81)	9.0 (8.0–10.0)	9.0 (8.0–9.69)
Ability to deal with bleeding	8.5	8.8	8.8
	8.5 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
In the oesophagus	8.6	8.7	8.7
	9.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
In the stomach	8.3	8.9	8.8
	8.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
Ability to deal with perforations	8.5	8.7	8.7
	8.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
In the oesophagus	8.3	8.4	8.4
	8.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
In the stomach	8.6	8.8	8.8
	9.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)

EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection; IQR: interquartile range.
Results are presented as mean and median (IQR 25–75%); Mann-Whitney test used as non-parametric test.

Table 4. The animal model as a learning tool.

Characteristics	Tutor ($n=13$) Mean Median (IQR)	Trainee ($n=78$) Mean Median (IQR)	Global ($n=91$) Mean Median (IQR)
Understanding how procedures are performed/coordination of tasks			
Oesophageal multiband EMR	8.8	8.9	8.8
	9.0 (8.0–10.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
Oesophageal ESD	8.6	8.2	8.3
	9.0 (8.0–9.0)	9.0 (7.0–9.0)	9.0 (7.0–9.0)
Gastric ESD	8.8	8.9	8.9
	9.0 (8.0–9.8)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
Complication detection and management	8.8	8.8	8.8
	9.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)

(continued)

Table 4. Continued

Characteristics	Tutor ($n = 13$) Mean Median (IQR)	Trainee ($n = 78$) Mean Median (IQR)	Global ($n = 91$) Mean Median (IQR)
Difficulty of procedures			
Oesophageal EMR using multiband mucosectomy	7.9	7.7	7.7
	8.0 (7.0–9.0)	8.0 (7.0–9.0)	8.0 (7.0–9.0)
Oesophageal ESD	7.4	6.5	6.7
	8.0 (7.0–9.0)	8.0 (3.5–9.0)	8.0 (4.0–9.0)
Gastric ESD	7.8	7.5	7.5
	8.0 (7.0–9.0)	8.0 (7.0–9.0)	8.0 (7.0–9.0)
Complication detection and management	8.2	8.1	8.1
	8.0 (8.0–9.0)	8.0 (7.0–9.0)	8.0 (7.0–9.0)
Usefulness of life animal simulated procedures			
Oesophageal multiband EMR	8.0	8.7	8.7
	9.0 (8.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)
Oesophageal ESD	7.6	8.9	8.6
	9.0 (7.0–9.0	10.0 (8.0–10.0)	9.5 (8.0–10.0)
Gastric ESD	8.1	9.1	8.9
	9.0 (8.0–9.0)	10.0 (8.8–10.0)	9.0 (8.0–10.0)
Complication detection and management	8.3	9.0	8.9
	9.0 (8.0–10.0)	9.5 (8.0–10.0)	9.0 (8.0–10.0)
Should a course like this be a prerequisite before clinical practice?			
Oesophageal multiband EMR	7.6	7.4	7.4
	8.0 (6.3–9.0)	9.0 (4.3–10.0)	9.0 (5.0–10.0)
Oesophageal ESD	8.4	9.2	9.0
	9.0 (8.3–9.0)	10.0 (9.0–10.0)	10.0 (9.0–10.0)
Gastric ESD	8.9	9.1	9.1
	9.0 (8.5–9.0)	10.0 (9.0–10.0)	10.0 (9.0–10.0)
Complication detection and management	8.3	8.1	8.1
	9.0 (8.0–9.0)	9.5 (6.0–10.0)	9.0 (6.0–10.0)

EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection; IQR: interquartile range.
Results are presented as mean and median (IQR 25–75%); Mann-Whitney test used as non-parametric test.

It is important to notice that in this work we have not addressed the effect of training in the animal model regarding outcomes in clinical practice. We believe that this objective should be a target for future studies.

In conclusion, EMR and ESD training in a live porcine model was considered very realistic compared to the human setting and was highly appreciated as a learning tool. This is the first study to establish face, content and expert validity of the live porcine model in performing multiband EMR, oesophageal and gastric ESD. The validation of this model provides the rationale to incorporate it into formal teaching programmes and provides a basis on which further studies can be conducted.

Acknowledgements

The authors would like to thank all of the participants in the workshops for their collaboration in filling out the questionnaires.

Declaration of conflicting interests

There are no conflicting interests to declare.

Ethics approval

The use of the live porcine model for training purposes in the workshops was approved by local Ethical Committees for the welfare of animals in medical training.

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

Informed consent

This validity study was not a research conducted on humans, although it was based on questionnaires answered by humans. An oral informed consent was obtained, based on the fact that the questionnaires were freely answered only by the health professionals themselves that attended the workshops and that the act of answering the questionnaires assumed their implicit acceptance/consent. A prerequisite of this approach was the complete anonymity of all participants.

References

1. Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. *Endoscopy* 2017; 49: 270–297.
2. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* 2015; 47: 829–854.
3. ASGE Technology Committee, Hwang JH, Konda V, Abu Dayyeh BK, et al. Endoscopic mucosal resection. *Gastrointest Endosc*. 2015; 82: 215–226.
4. Komeda Y, Bruno M and Koch A. EMR is not inferior to ESD for early Barrett's and EGJ neoplasia: An extensive review on outcome, recurrence and complication rates. *Endosc Int Open* 2014; 2: E58–E64.
5. van Vilsteren FG, Pouw RE, Herrero LA, et al. Learning to perform endoscopic resection of esophageal neoplasia is associated with significant complications even within a structured training program. *Endoscopy* 2012; 44: 4–12.
6. Oka S, Tanaka S, Kaneko I, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. *Gastrointest Endosc* 2006; 64: 877–883.
7. Pimentel-Nunes P, Mourao F, Veloso N, et al. Long-term follow-up after endoscopic resection of gastric superficial neoplastic lesions in Portugal. *Endoscopy* 2014; 46: 933–940.
8. Choi IJ, Kim CG, Chang HJ, et al. The learning curve for EMR with circumferential mucosal incision in treating intramucosal gastric neoplasm. *Gastrointest Endosc* 2005; 62: 860–865.
9. Oda I, Odagaki T, Suzuki H, et al. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. *Dig Endosc* 2012; 24: S129–S132.
10. Yamamoto Y, Fujisaki J, Ishiyama A, et al. Current status of training for endoscopic submucosal dissection for gastric epithelial neoplasm at Cancer Institute Hospital, Japanese Foundation for Cancer Research, a famous Japanese hospital. *Dig Endosc* 2012; 24: S148–S153.
11. Coman RM, Gotoda T and Draganov PV. Training in endoscopic submucosal dissection. *World J Gastrointest Endosc* 2013; 5: 369–378.
12. Oyama T, Yahagi N, Ponchon T, et al. How to establish endoscopic submucosal dissection in Western countries. *World J Gastroenterol* 2015; 21: 11209–11220.
13. Deprez PH, Bergman JJ, Meisner S, et al. Current practice with endoscopic submucosal dissection in Europe: Position statement from a panel of experts. *Endoscopy* 2010; 42: 853–858.
14. Berr F, Ponchon T, Neureiter D, et al. Experimental endoscopic submucosal dissection training in a porcine model: Learning experience of skilled Western endoscopists. *Dig Endosc* 2011; 23: 281–289.
15. Parra-Blanco A, Arnau MR, Nicolas-Perez D, et al. Endoscopic submucosal dissection training with pig models in a Western country. *World J Gastroenterol* 2010; 16: 2895–2900.
16. Vazquez-Sequeiros E, de Miquel DB, Olcina JR, et al. Training model for teaching endoscopic submucosal dissection of gastric tumors. *Rev Esp Enferm Dig* 2009; 101: 546–552.
17. Streiner DL, Norman GR and Cairney J. Health measurement scales. 5th ed. Oxford: Oxford University Press, 2015, pp.23-24, 79: 227–233.
18. Keszei AP, Novak M and Streiner DL. Introduction to health measurement scales. *J Psychosom Res* 2010; 68: 319–323.
19. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol* 2010; 63: 737–745.
20. Koch AD, Haringsma J, Schoon EJ, et al. A second-generation virtual reality simulator for colonoscopy: Validation and initial experience. *Endoscopy* 2008; 40: 735–738.
21. Buzink SN, Koch AD, Heemskerk J, et al. Acquiring basic endoscopy skills by training on the GI Mentor II. *Surg Endosc* 2007; 21: 1996–2003.
22. van der Wiel SE, Kuttner Magalhaes R, Rocha Goncalves CR, et al. Simulator training in gastrointestinal endoscopy – From basic training to advanced endoscopic procedures. *Best Pract Res Clin Gastroenterol* 2016; 30: 375–387.
23. Hochberger J, Maiss J, Magdeburg B, et al. Training simulators and education in gastrointestinal endoscopy: Current status and perspectives in 2001. *Endoscopy* 2001; 33: 541–549.
24. Wang TE, Wang HY, Lin CC, et al. Simulating a target lesion for endoscopic submucosal dissection training in an ex vivo pig model. *Gastrointest Endosc* 2011; 74: 398–402.
25. Bok GH and Cho JY. ESD hands-on course using ex vivo and in vivo models in South Korea. *Clin Endosc* 2012; 45: 358–361.
26. Horii J, Goto O, Shimoda M, et al. Which part of a porcine stomach is suitable as an animal training model for gastric endoscopic submucosal dissection? *Endoscopy* 2016; 48: 188–193.
27. Herreros de Tejada A. ESD training: A challenging path to excellence. *World J Gastrointest Endosc* 2014; 6: 112–120.
28. Yamamoto S, Uedo N, Ishihara R, et al. Endoscopic submucosal dissection for early gastric cancer performed

by supervised residents: Assessment of feasibility and learning curve. *Endoscopy* 2009; 41: 923–928.
29. Martinek J, Stefanova M, Suchanek S, et al. Training of different endoscopic skills on ex-vivo animal model. *Simul Healthc* 2014; 9: 112–119.
30. Gerson LB and Van Dam J. Technology review: The use of simulators for training in GI endoscopy. *Gastrointest Endosc* 2004; 60: 992–1001.

B) LEARNING CURVE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION

A STEEP EARLY LEARNING CURVE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN THE LIVE PORCINE MODEL.

Küttner-Magalhães R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD.

Dig Dis. 2021. doi:10.1159/000521429.

Digestive Diseases

Endoscopy and Imaging: Research Article

Dig Dis
DOI: 10.1159/000521429

Received: March 9, 2021
Accepted: December 8, 2021
Published online: December 14, 2021

A Steep Early Learning Curve for Endoscopic Submucosal Dissection in the Live Porcine Model

Ricardo Küttner-Magalhães[a, b] Mário Dinis-Ribeiro[c, d] Marco J. Bruno[e]
Ricardo Marcos-Pinto[a, b, d] Carla Rolanda[f, g, h] Arjun D. Koch[e]

[a]Department of Gastroenterology, Santo António Hospital, Porto University Hospital Center, Porto, Portugal; [b]Institute of Biomedical Sciences Abel Salazar, University of Porto, Porto, Portugal; [c]Department of Gastroenterology, Portuguese Oncology Institute of Porto, Porto, Portugal; [d]Department of Community Medicine, Health Information and Decision (MEDCIDS) and CINTESIS, Faculty of Medicine of Porto, Porto, Portugal; [e]Department of Gastroenterology and Hepatology, Erasmus MC Cancer Institute, University Medical Center, Rotterdam, The Netherlands; [f]Department of Gastroenterology, Braga Hospital, Braga, Portugal; [g]Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal; [h]ICVS/3B's, PT Government Associate Laboratory, Braga/Guimarães, Portugal

Keywords
Endoscopic submucosal dissection · Gastrointestinal endoscopy · Learning curve · Animal models · Simulation · Training

Abstract
Background: Endoscopic submucosal dissection (ESD) is a demanding procedure requiring high level of expertise. ESD training programs incorporate procedures with live animal models. This study aimed to assess the early learning curve for performing ESD on live porcine models by endoscopists without any or with limited previous ESD experience. ***Methods:*** In a live porcine model ESD workshop, number of resections, completeness of the resections, en bloc resections, adverse events, tutor intervention, type of knife, ESD time and size of resected specimens were recorded. ESD speed was calculated. ***Results:*** A total of 70 procedures were carried out by 17 trainees. The percentage of complete resections, en bloc resections and ESD speed increased from the first to the latest procedures (88.2%–100%, 76.5%–100%, 8.6–31.4 mm^2/min, respectively). The number of procedures in which a trainee needed tutor intervention and the number of adverse events also decreased throughout the procedures (4 to 0 and 6 to 0, respectively). During the workshop, when participants changed to a different type of knife, ESD speed slightly decreased (18.5 mm^2/min to 17.0 mm^2/min) and adverse events increased again (0–2). ***Conclusions:*** Through successive procedures, complete resections, en bloc resections, and ESD speed improve whereas adverse events decrease, supporting the role of the live porcine model in the preclinical learning phase. Changing ESD knives has a momentarily negative impact on the learning curve.

Introduction

Endoscopic submucosal dissection (ESD) is a demanding technique that enables high en bloc resection rates, R0 resections and low rate of local recurrences regardless of lesion size as well as an accurate tumor histopathological

karger@karger.com
www.karger.com/ddi

Karger
OPEN ACCESS

Correspondence to:
Arjun D. Koch, a.d.koch@erasmusmc.nl

staging and grading with precise evaluation of resection margins [1–8]. On the other hand, it is associated with long procedure times and considerable risk of adverse events (such as bleeding and perforation) [9–11]. In addition, ESD has a difficult and prolonged learning curve [5, 9, 12, 13]. ESD training programs include acquiring basic knowledge, practicing on animal models (both ex vivo and in vivo models), visiting centers with a high ESD volume, attendance of hands-on training ESD workshops and only then proceeding to clinical practice, ideally under supervision of an expert during the first cases [14–18].

This is particularly relevant in Western settings where the number of ESD experts is limited and the possibility of starting ESD in superficial gastric neoplasms, which are the easiest and safest procedures, is limited due to the low prevalence of such lesions [5, 9, 12, 13]. Workshops using animal models are organized in training centers with the potential to improve the learning process and achieve initial competence in ESD [19–22]. This study aimed to assess the early learning curve for performing ESD on live porcine models by endoscopists without any or with limited previous ESD experience.

Methods

Study Design

This prospective study was conducted during a workshop for ESD training, co-organized by the European Association for Gastroenterology, Endoscopy and Nutrition (EAGEN) and the European Society of Gastrointestinal Endoscopy (ESGE). It included theoretical lectures and hands-on practice with live porcine models. The workshop had duration of 2 days and took place in the training center of the Erasmus School of Endoscopy at the Erasmus University Medical Center in Rotterdam, the Netherlands.

Animal Model

The use of the live porcine model for training purposes in the workshop was approved by local Ethical Committee for the welfare of animals in medical training. It was conducted under the National Experiments on Animals Act, revised in 2014 to implement the European Directive 2010/63 protecting animals used in research. Animal welfare and regulatory compliance were overseen by local Animal Welfare Body and government inspectors on behalf of the authorities (project license NL license # AVD1010020173286).

Procedures were conducted in accordance with the "Animal Research: Reporting of in vivo Experiments" (ARRIVE) Guidelines [23]. Live pigs (*Sus scrofus domesticus*), weighing between 30 and 40 kg were used. Animals were given a liquid diet for 3 days and fasted for 8 h before the procedures. According to local protocol, with the support of the veterinarian staff throughout the course, general anesthesia with endotracheal intubation and mechanical ventilation was performed. Drugs were employed in the following sequence: premedication – ketamine 25–35 mg/kg IM and midazolam 1 mg/kg IM; induction – propofol 0.5–1 mg/kg IV; maintenance – isoflurane 1.5–2.5% ET PO, sufentanil 0.3–0.5 μg/kg IV, NaCl 0.9% 10 g/kg IV or gelofusine, propofol, and sufentanil as required. Animals were euthanized with pentobarbital overdose.

Participants

Trainees attending the workshop for ESD training were evaluated. Demographic data and previous endoscopic experience were collected. Identity protection and confidentiality of the collected data were guaranteed. Only the ones who wished to do so responded willingly and all had the possibility of not doing it if they wished. Accordingly, participant's acceptance/consent was implicit, and written informed consent was not necessary.

Procedures

Standard Pentax® (Tokyo, Japan) flexible endoscopes and ERBE® (Tübingen, Germany) VIO 200s and VIO3 electrosurgical units were used. A soft, straight distal attachment cap from Olympus® (Tokyo, Japan) was mounted on the tip of the endoscope.

Direct assistance was assured by one of the participants, who acted according to the instructions of the endoscopist performing the procedure. International experts supervised this assistance and all the steps of the procedure, giving verbal instructions and intervening when deemed necessary (Fig. 1). All of them were highly experienced in clinical ESD (more than 10 years of continuous clinical practice) and in supervising ESD training courses (more than 5 years of continuous tutor practice).

Gastric ESD was conducted using ERBE® HybridKnives® (Tübingen, Germany) coupled with a high-pressure injection system, ERBERJET 2® (Tübingen, Germany) which allows for cutting, coagulation and submucosal injection with the same knife. The injection solution was physiological saline with a few drops of indigo carmine.

During the first procedures, the HybridKnife® I-type (which is a noninsulated needle-type knife) was used and during following procedures the HybridKnife® O-type (which is a partially insulated tip knife). Trainees were instructed to choose a place in the gastric mucosa, mark the outer margins of a pseudo-lesion with the tip of the knife, perform submucosal injection, and create a circumferential incision, followed by submucosal dissection and re-lifting the pseudo-lesion when needed. Bleedings were treated using submucosal injection, by coagulation with the knife, by using a bipolar hemostatic forceps, HemoStat-Y®, Pentax® (Tokyo, Japan) or by clip application, Instinct clip®, Cook Medical® (Winston-Salem, NC, USA). Resected specimens were retrieved at the end of each procedure, carefully stretched to in vivo size, and measured by an independent observer (RKM). Procedures were performed over the 2 days of the workshop.

Assessment

Parameters related to gastric ESD performance like number of resections, completeness of the resection (ability to completely resect the lesion), en bloc resection (ability to completely resect the lesion en bloc with all markings visible on the specimen), adverse events (intraprocedural bleeding and perforation), tutor intervention, procedure time (from the first submucosal injection after marking to the complete removal of the pseudo lesion), and size of resected specimens were recorded for each procedure. Only significant continued bleeding that did not subside spontaneously or with coagulation from the tip of the ESD knife and required the use of an hemostatic forceps or endoclip was considered an intraprocedural bleeding. Tu-

Fig. 1. Live porcine model endoscopy workstation.

Table 1. Background characteristics and endoscopic experience of participants

Age (years), median (IQR); mean (SE)	40 (36–47); 42 (6.5)
Gastroenterologists, *n* (%)	15 (88)
Academic or tertiary hospital, *n* (%)	9 (53)
Fully trained physicians, *n* (%)	15 (88)
Previous endoscopic experience	
Years performing endoscopy, median (IQR); mean (SE)	10 (6–15); 11.2 (4.8)
Colonoscopies: ≥201/year; ≥601 total, *n* (%)	13 (76); 14 (82)
Upper endoscopies: ≥201/year; ≥601 total, *n* (%)	14 (82); 14 (82)
ERCP: ≥1/year; ≥101 total, *n* (%)	7 (41); 9 (53)
EUS: ≥1/year; ≥201 total, *n* (%)	7 (41); 6 (35)
Esophageal EMR: ≥1/year; ≥21 total, *n* (%)	12 (71); 8 (47)
Gastric EMR: ≥1/year; ≥21 total, *n* (%)	14 (82); 10 (59)
Colonic EMR: ≥1/year; ≥21 total, *n* (%)	14 (82); 13 (76)
Colonic EMR: ≥21/year; ≥51 total, *n* (%)	11 (65); 12 (71)
EMR: inject and snare technique, *n* (%)	15 (88)
EMR: band and snare technique, *n* (%)	12 (71)
EMR: cap and snare technique, *n* (%)	12 (71)
ESD: ≥1/year; ≥1 ESD total, *n* (%)	4 (24); 5 (29)

EMR, endoscopic mucosal resection; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; SE, standard error.

tor intervention was defined as a short hands-on assistance in procedures in which the tutor deemed it necessary, after which the endoscope was handed back to the trainee. Verbal guidance was allowed at any time during the workshop and was not recorded.

The type of knife used was documented. The surface area of the resected specimen was calculated using a pre-specified formula: surface area (mm^2) = largest diameter of specimen (mm) × smallest diameter of specimen (mm) × 0.25 × π. ESD speed was calculated accordingly: speed (mm^2/min) = surface area (mm^2) of resected specimen/time of procedure (min).

Statistical Analysis

The IBM Statistical Package for Social Sciences (SPSS Version 25.0.0; SPSS Inc, Chicago, IL, USA) was used for data analysis. Descriptive statistics were determined for all measures according to type of variables. Proportions were reported for dichotomous and ordinal variables. For continuous variables, the medians (with interquartile range [IQR] 25–75) or means (with standard error) were described. Nonparametric tests were used to assess statistical differences (Wilcoxon signed-rank test). Proportions were compared with the χ^2 test. Significance level was defined as $p < 0.05$.

Results

From the 17 participants, background characteristics and endoscopic experience were obtained for 15 and are summarized in Table 1. Their median age was 40 years (IQR, 36–47). A total of 70 procedures (P) were performed by 17 trainees (Table 2). Each trainee performed a median of 4 procedures (IQR, 3.5–5.0).

Dig Dis
DOI: 10.1159/000521429

Table 2. ESD procedures

	P1	*p* value (P1 vs. P2)	P2	*p* value (P2 vs. P3)	P3	*p* value (P3 vs. P4)	P4	*p* value (P4 vs. P5)	P5	*p* value (P5 vs. P6)	P6
N	17		17		16		13		6		1
Complete resection, *n*/*N* (%)	15/17 (88.2)	1.000	15/17 (88.2)	0.163	16/16 (100)	N/A	13/13 (100)	N/A	6/6 (100)	N/A	1/1 (100)
En bloc resection, *n*/*N* (%)	13/17 (76.5)	0.378†	15/17 (88.2)	0.163†	16/16 (100)	N/A	13/13 (100)	N/A	6/6 (100)	N/A	1/1 (100)
Tutor intervention, *n*	4	0.378†	2	0.163†	0	0.267	1	0.497	0	N/A	0
Type of knife-*n*	I-17		I-15 O-2		I-13 O-3		I-5 O-8		I-6		I-1
Change of knife (*n*)	No		Yes (2)		Yes (3)		Yes (8)		No		No
Time, min, median (IQR)	39.0 (29.0–47.5)	0.704†	34.0 (18.5–49.5)	0.010†	21.0 (13.5–23.0)	0.969	20.0 (14.5–24.0)	0.598	17.0 (13.5–25.5)	N/A	9.0
Area /surface, mm^2, median (IQR)	263.9 (188.5–408.4)	0.094	392.7 (281.0–494.8)	0.650	312.2 (192.2–404.5)	0.675	296.9 (213.2–395.0)	0.116	412.3 (266.3–645.4)	N/A	282.7
Speed, mm^2/min, median (IQR)	8.6 (4.5–13.4)	0.006	14.8 (7.5–19.0)	0.100	18.5 (8.5–23.7)	0.152	17.0 (13.0–17.8)	0.028	24.7 (17.6–33.1)	N/A	31.4
Bleeding, *n*	3	0.297	1	0.331	0	N/A	0	N/A	0	N/A	0
Perforation, *n*	3	0.638	2	0.163	0	0.1099	2	0.3226	0	N/A	0

I, I-type, noninsulated tip, ERBE HybridKnife; O, O-type, partially insulated tip, ERBE HybridKnife; P, Procedure; N/A, not applicable. † No statistically difference was observed between P1 and P2, but it was noted when P1 was compared to P3 (P1 vs. P3, $p < 0.05$).

The percentage of complete resections was 88.2% in the first 2 procedures and 100% in the following ones. En bloc resections improved from 76.5% and 88.2% in the first 2 procedures respectively, to 100% during the subsequent procedures (P1 vs. P3, $p < 0.042$). The number of procedures in which a trainee needed hands-on intervention from the tutor also decreased throughout the procedures (4 in P1, 2 in P2 to 0 in P5 and P6; P1 vs. P3, $p < 0.042$). Median ESD speed increased from the first to the latest procedures: 8.6 mm^2/min in P1 to 14.8 mm^2/min in P2 (P1 vs. P2, $p = 0.006$), 24.7 mm^2/min in P5 (P4 vs. P5, $p = 0.028$) and 31.4 mm^2/min in P6. In contrast, ESD time decreased: 39 min in P1 to 34 min in P2, 21 min in P3 (P1 vs. P3, $p = 0.002$; P2 vs. P3, $p = 0.01$) and 9 min in P6. No significant variation in specimen's area occurred comparing successive procedures.

The first procedures were all performed with the noninsulated tip HybridKnife I-type. After 1 to 3 procedures, all trainees switched to the HybridKnife O-type.

Adverse events decreased throughout procedures (3 bleedings and 3 perforations in the P1 to 0 in P5 and P6). In total, there were 7 perforations (10%) and 4 bleedings (5.7%), managed with endoclips and hemostatic forceps. Perforations in P1 and P2 occurred with type I while perforations in P4 occurred with the O type. When a great number of participants ($n = 8$) changed to a different type of knife (P4), ESD speed slightly temporarily decreased (18 5 mm^2/min on P3 to 17.0 mm^2/min on P4) and the number of perforations increased again (0 on P3 to 2 on P4) (Fig. 2).

Discussion

In this study, we have demonstrated that through successive procedures within a hands-on training program, en bloc resection rates and ESD speed increase whereas adverse events decrease. Changing to a different ESD knife has a momentarily negative impact on the learning curve.

ESD training programs include hands-on practicing in live animal models [14–17]. Face, expert, and content validity of the live porcine model in training for endoscopic mucosal resection and ESD have been established in a previous study. This model is considered very realistic and procedures accurately resemble human cases. Moreover, the simulation process is highly appreciated as a learning tool [19]. Current virtual reality and mechanical simulators are not suitable for training advanced endoscopic resection due to the inability to sufficiently repro-

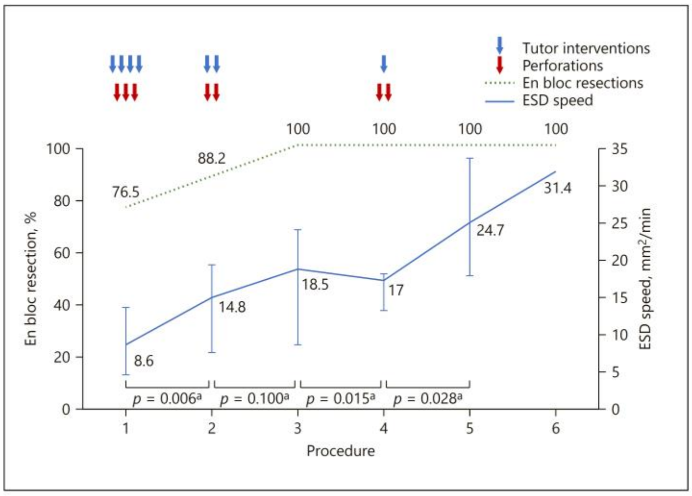

Fig. 2. En bloc resections and ESD speed. [a] p values refer to ESD speed comparisons; error bars on ESD speed represent IQR (25–75).

duce tissue properties like elasticity and tactile feedback resembling human tissue [24].

In general, the skill-lab setting with animal models provide the opportunity to train team coordination between the endoscopist and assistant, to gain familiarity with the devices and electrosurgical units, to adequate handle and position the scope and to rehearse the kind of movements typical and crucial to ESD, improving tip control [20, 25].

Some authors support the idea that ex vivo training is not sufficient to simulate clinical practice and that in vivo training is essential [26, 27]. Live animal models can achieve those characteristics and add breathing movements, heartbeats, peristalsis, intraluminal secretions and tissue reaction to injection, and electrocautery, which makes them closely related to the human setting. In addition, dealing with intraprocedural complications, such as bleedings and perforations can be trained as close as it gets to the human situation [15, 19, 25, 27, 28]. On the downside, availability of and the need to sacrifice animals, dedicated facilities, equipment, veterinarian support, and costs represent the disadvantage of the model [15, 25, 27–29]. For these reasons, ex vivo models are probably adequate in the initial learning phase and animal models should be reserved only for the subsequent stage of preclinical training.

A previous study demonstrated that the mean resection time was significantly diminished for porcine gastric ESDs in the second half of the cases, although all procedures were carried out by a single endoscopist and both ex vivo and in vivo models were used [25]. In an ex vivo model, performing 30 gastric ESDs led to decreased procedure times, a lower perforation rate and improvement in en bloc resection rate [30]. In ex vivo stomach pig models, to achieve a predefined level of competence, trainees needed 23–25 procedures in one study [31]. In a bovine ex vivo model, an ESD goal was achieved by 71% of trainees in a software learning group (84% at the 30th procedure) and 61% in the control group (50% at the 30th procedure) [32]. In a bovine ex vivo model, complete resections were achieved in 92%, with 89% en bloc. Perforations occurred in 6% and the mean procedure time was 33 min with an average dissection speed of 5.2 mm^2/min [33]. A study on ex vivo porcine colonic model, with an overall en bloc resection of 94.4% and perforation of 14.4%, demonstrated an inflexion of the learning curve at the 9th ESD procedure [34]. A summary of the studies is presented in Table 3.

In our study, we highlight that we addressed ESD speed (which increased throughout the procedures), instead of time or surface area alone. We find that the increment in speed better reflects the acquisition of skills or learning curve of the trainee. The use of only a single parameter-like procedure time or surface area is a poor measure for improved performance because these measures are highly related to each other. It will take more time to resect a larger lesion and vice versa. Another important observation is that the rate of adverse events did

Dig Dis
DOI: 10.1159/000521429

Table 3. Studies on training in ESD

Study [ref.]	Type of model	Organ	ESDs, *n*	Complete resection, *n* (%)	En bloc resection, *n* (%)	Time, min, mean (SD) or median (IQR)	Area/surface, mm^2, mean (SD) or median (IQR)	Speed, mm^2/min, mean (SD) or median (IQR)	Bleeding, *n/N* (%)	Perforation, *n/N* (%)	Key findings
Parra-Blanco et al. [25]	In and ex vivo, porcine	Stomach and esophagus	30	28 (93.3)	27 (90)	81.3 (46.6); for gastric cases: 98.9 (62.4) 1st 13 ESDs; 61.7 (17.6) latest 8 ESDs	Mean size 45.2 mm (17.8)	NA	5/22 in vivo (22.7)	1/22 in vivo (4.5)	For gastric ESD, mean time was significantly longer in the first half of the study than in the second half
Kato et al. [30]	Ex vivo, porcine	Stomach	120 (beginners)	120 (100)	53/60 (88.3) 1st 30 ESDs to 60/60 (100) 2nd 30 ESDs	32.8 (NA) 1st 30 ESDs; 15.2 min (NA) 2nd 30 ESDs	868 1st 30 ESDs; 859 2nd 30 ESDs	26.4 1st 30 ESDs; 56.7 2nd 30 ESDs	NA	8/120 (6.7) total; 8 in 1st 30 ESDs; 0 2nd 30 ESDs	After 30 ESD cases, procedure time decreased, en bloc resection of 100% and no perforation were achieved
Bhatt et al. [31]	Ex vivo, porcine	Stomach	55	NA	38 (69.1) total 5/20 (25) 1st 20 ESDs; 18/20 (90) 2nd 20 ESDs; 15/15 (100) latest 15 ESDs	39.0 (30.0–58.0); 60.0 (51.0–65.0) 1st 20 ESDs; 36.5 (31.5–45.0) 2nd20 ESDs; 28.0 (19.0–33.0) latest 15 ESDs	NA	NA	NA	8/55 (14.5) total 3/20 (15.0) 1st 20 ESDs; 5/20 (25) 2nd 20 ESDs; 0/15 latest 15 ESDs	Endoscopist 1 reached competency at 23 procedures; endoscopist 2 reached competency at 25 procedures Competency was defined as consistent en bloc resection of a 30 mm area within 30 min without perforation
Pioche et al. [32]	Ex vivo, bovine	Colon	1,170	797 (68.1) total; 414/544 (76.1) software group; 383/569 (67.3) control group; only for procedures <75 min	NA	34.1 (13.4) software group; 32.3 (14.0) control group	NA	52 (29) software group; 64 (36) control group	NA	51/1,113 (4.6) total; 22/544 (4) software group; 29/569 (5.1) control group; only for procedures <75 min	Success was achieved in 70.9% in the software group and 61.2% in the control group For the 30th procedure, the rate of complete resection was superior in the software group (84.2%) compared with the control group (50.0%) Software group used self-learning software. Control group observed an ESD procedure video Successful ESD: complete en bloc resection without any perforation performed in less than 75 min

Table 3 (continued)

Study [ref.]	Type of model	Organ	ESDs, *n*	Complete resection, *n* (%)	En bloc resection, *n* (%)	Time, min, mean (SD) or median (IQR)	Area/surface, mm^2, mean (SD) or median (IQR)	Speed, mm^2/min, mean (SD) or median (IQR)	Bleeding, *n/N* (%)	Perforation, *n/N* (%)	Key findings
Pioche et al. [33]	Ex vivo, bovine	Colon	64	59 (92.2)	57 (89.1)	33.3 (15.6)	1,500 (370)	52 (20)	NA	4/64 (6.2)	Adult bovine colon model is more homogenous than a calf: with calf colons, failure rates were higher and speed was lower Time procedure decreased throughout the study A learning curve appeared at the speed of 49 and 59 mm^2/min
Gromski et al. [34]	Ex vivo, porcine	Colon	90	NA	85 (94.4)	49.6 (29.6)	NA	NA	NA	13 (14.4)	Significant improvement after 9th ESD Suggestion of at least 9 ex vivo procedures prior to live animal or proctored colonic ESD training
Teoh et al. [36]	In vivo, porcine	Stomach, esophagus	32 total; 23 gastric; 9 esophageal	NA	NA	52.09 (24.67) gastric ESD; 32.50 (8.45) esophageal ESD	Mean size 266 mm (118)	NA	13/32 (40.6)	20/32 (62.5) total; 15 gastric (65.2); 5 esophageal (55.6)	High rate of complications: in gastric ESD, 65.2% and 56.5% of participants had perforations and bleedings, respectively There was a higher proportion of perforations with noninsulated knives
Kasapidis et al. [21]	In vivo, porcine	Gastric	76	NA	72 (94.7)	48 (4.4) 1st day; 43 (4.8) 2nd day	NA	138 (20) 1st day; 163 (23) 2nd day	9/76 (11.8) total; 5 1st day; 4 2nd day	4/76 (5.3) total; 2 1st day; 2 2nd day	ESD time and cutting speed differed significantly between the 1st and 2nd day Similar adverse events between the 1st and 2nd day
Chapelle et al. [22]	In vivo, porcine	Gastric	58	58 (100)	58 (100)	46 (NA) in ESD2; 78 (NA) in ESD4	488 (NA) in ESD2; 2,634 (NA) in ESD4	9.7 (4.8–15.7) in ESD1; 30.4 (14.3–37.0) in ESD4	2/58 (3.4)	3/58 (5.2)	Increase in ESD speed marked between the first 2 ESDs compared with the 4th and 5th Improved endoscopist capability from the 3rd ESD

NA, not available; SD, standard deviation.

not increase when trainees started performing faster ESDs. The number of adverse events decreased as performance and speed improved during the learning phase.

ESD speed in live models varies between studies from means of 5–10 mm^2/min [35] in the first procedures to 22–30 mm^2/min [21, 22] in the later ones. This is in line with our results that varied from median 8.6 mm^2/min in the first procedure to 24.7 mm^2/min and 31.4 mm^2/min in the last ones.

We observed a momentarily decrease in ESD speed and a slight increase in perforation number when trainees switched to a different knife with different properties. Complete and en bloc resection rates were unaffected. ESD performance improved up to that point and introducing a new type of knife immediately had a negative impact on ESD performance. This finding supports the idea that each individual has to get used to a particular type of knife and changing it leads to an adaptive phase. This phenomenon was observed despite the fact that we switched to a potentially "safer" knife because of its partial insulation at the tip. Therefore, we collected supporting evidence for one key informal advice that ESD experts often provide, which is to maintain experience with the same knife and not change frequently the type of knife used.

There were 7 perforations which correspond to 10% of the procedures. This denotes the difficulty of the technique and is in line with other published studies: 5.2–62.5% [21, 22, 36] in live animal models and 4.6–14.5% in ex vivo models [30–34].

The fact that a plateau phase was not reached in this study is in all likelihood related to the limited number of ESD procedures performed by each endoscopist and supports the need and rationale for further training in the animal model. A minimum of 10–30 ESD procedures in the animal model is suggested, before moving to human cases [14, 30, 37]. This study supports this conclusion and the importance of using live porcine models to train endoscopists in ESD.

Concerning the strengths of this study, we highlighted its prospective design, the objective nature of the parameters that were assessed by an independent observer and the diverse origin and background of the trainees. This supports the generalization of the results. It is also important to emphasize that ESD performance improved dramatically in a 2 days course and that each knife is operated differently.

With regard of limitations, we stress that trainees can have different background characteristics and distinct skills and learning curves. We underline the limited number of procedures, the fact that locations on the pig stomach were not assessed and that the porcine colon was not included. Tutors varied from different groups, although presenting similar characteristics. Also, procedures were performed on healthy tissue with no pathological findings, as opposed to clinical practice, where neoplastic changes might affect submucosal tissue and thereby hampering submucosal dissection. Nevertheless, this is a known limitation of training in porcine model, but still experts agree that it represents the closest resemblance possible to the human setting, as was previously demonstrated [19].

In conclusion, training in live animal models improves ESD performance measures supporting its role in teaching programs. Distinct ESD knives are operated differently.

Acknowledgments

We would like to thank all the participants in the workshops for their collaboration.

Statement of Ethics

The workshop was approved by the local Ethics Committee of Erasmus MC, University Medical Center, Rotterdam, The Netherlands, for the welfare of animals in medical training (Ref. No. AVD1010020173286). It was conducted under the National Experiments on Animals Act, revised in 2014 to implement the European Directive 2010/63 protecting animals used in research. Procedures were conducted in accordance with the "Animal Research: Reporting of in vivo Experiments" (ARRIVE) Guidelines. Only the endoscopists who wished to participate did it willingly and all had the possibility of not doing it if they wished. Invitees were informed that data would be analyzed and participation was voluntary. Identity protection and confidentiality of the collected data were guaranteed according to General Data Protection Regulation. Accordingly and in agreement with the Ethics Committee, completing the questionnaire implied the participant's implicit acceptance/consent. Therefore, the requirement for written informed consent was waived.

Conflict of Interest Statement

Ricardo Küttner-Magalhães, Ricardo Marcos-Pinto, and Carla Rolanda have no conflicts of interest or financial ties to disclose. Mário Dinis-Ribeiro reports research grants from Olympus and Fujifilm. Marco J. Bruno reports consultant support for industry and investigator-initiated studies from Boston Scientific and Cook Medical, consultant support for investigator-initiated studies from Pentax Medical, Mylan, ChiRoStim, and 3M. Arjun D. Koch reports speaker fees from Cook Medical, ERBE, Pentax and Boston Scientific.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or nonprofit sectors. The workshop that allowed the present study was unrestrictedly sponsored by Pentax® (Tokyo, Japan), ERBE® (Tübingen, Germany), and Cook Medical® (Winston-Salem, NC, USA) which provided flexible endoscopes, electrosurgical units, and endoscopic devices. The sponsors had no influence on the scientific content of the workshop neither on this study.

Author Contributions

All authors have contributed and agreed on the content of the manuscript. Ricardo Küttner-Magalhães contributed to the study conception, study design, data acquisition, data analysis, data interpretation, manuscript writing, and critical revision. Mário Dinis-Ribeiro contributed to the study conception, study design, study supervision, data analysis, data interpretation, and critical revision of the manuscript. Marco J. Bruno contributed to the study conception, study design, and critical revision of the manuscript. Ricardo Marcos-Pinto contributed to data interpretation and critical revision of the manuscript. Carla Rolanda contributed to the study conception and design, data interpretation, and critical revision of the manuscript. Arjun D. Kock contributed to the study conception and design, study supervision, data analysis, data interpretation, and critical revision of the manuscript. All authors read and approved the final version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Toyonaga T, Nishino E, Man-I M, East JE, Azuma T. Principles of quality controlled endoscopic submucosal dissection with appropriate dissection level and high quality resected specimen. Clin Endosc. 2012;45(4):362–74.
2 Kakushima N, Fujishiro M. Endoscopic submucosal dissection for gastrointestinal neoplasms. World J Gastroenterol. 2008;14(19):2962–7.
3 Nakamoto S, Sakai Y, Kasanuki J, Kondo F, Ooka Y, Kato K, et al. Indications for the use of endoscopic mucosal resection for early gastric cancer in Japan: a comparative study with endoscopic submucosal dissection. Endoscopy. 2009;41(9):746–50.
4 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(11):933–40.
5 Terasaki M, Tanaka S, Oka S, Nakadoi K, Takata S, Kanao H, et al. Clinical outcomes of endoscopic submucosal dissection and endoscopic mucosal resection for laterally spreading tumors larger than 20 mm. J Gastroenterol Hepatol. 2012;27(4):734–40.
6 Lee EJ, Lee JB, Lee SH, Youk EG. Endoscopic treatment of large colorectal tumors: comparison of endoscopic mucosal resection, endoscopic mucosal resection-precutting, and endoscopic submucosal dissection. Surg Endosc. 2012;26(8):2220–30.
7 Saito Y, Fukuzawa M, Matsuda T, Fukunaga S, Sakamoto T, Uraoka T, et al. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. Surg Endosc. 2010;24(2):343–52.
8 Oka S, Tanaka S, Kaneko I, Mouri R, Hirata M, Kawamura T, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. Gastrointest Endosc. 2006;64(6):877–83.
9 Toyokawa T, Inaba T, Omote S, Okamoto A, Miyasaka R, Watanabe K, et al. Risk factors for perforation and delayed bleeding associated with endoscopic submucosal dissection for early gastric neoplasms: analysis of 1,123 lesions. J Gastroenterol Hepatol. 2012;27(5):907–12.
10 Yoshida N, Wakabayashi N, Kanemasa K, Sumida Y, Hasegawa D, Inoue K, et al. Endoscopic submucosal dissection for colorectal tumors: technical difficulties and rate of perforation. Endoscopy. 2009;41(9):758–61.
11 Moss A, Bourke MJ, Williams SJ, Hourigan LF, Brown G, Tam W, et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology. 2011;140(7):1909–18.
12 Probst A, Golger D, Anthuber M, Märkl B, Messmann H. Endoscopic submucosal dissection in large sessile lesions of the rectosigmoid: learning curve in a European center. Endoscopy. 2012;44(7):660–7.
13 Oda I, Odagaki T, Suzuki H, Nonaka S, Yoshinaga S. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc. 2012;24(Suppl 1):129–32.
14 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(9):829–54.
15 Coman RM, Gotoda T, Draganov PV. Training in endoscopic submucosal dissection. World J Gastrointest Endosc. 2013;5(8):369–78.
16 Oyama T, Yahagi N, Ponchon T, Kiesslich T, Berr F. How to establish endoscopic submucosal dissection in Western countries. World J Gastroenterol. 2015;21(40):11209–20.
17 van der Wiel SE, Küttner Magalhães R, Rocha Gonçalves CR, Dinis-Ribeiro M, Bruno MJ, Koch AD. Simulator training in gastrointestinal endoscopy: from basic training to advanced endoscopic procedures. Best Pract Res Clin Gastroenterol. 2016;30(3):375–87.
18 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(10):980–92.
19 Kuttner-Magalhaes R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD. Training in endoscopic mucosal resection and endoscopic submucosal dissection: face, content and expert validity of the live porcine model. United European Gastroenterol J. 2018;6(4):547–57.
20 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(4):281–9.
21 Kasapidis P, Bassioukas S, Mavrogenis G, Tribonias G, Delis K, Georgopoulos S, et al. Experimental gastric endoscopic submucosal dissection: training in a porcine model. Ann Gastroenterol. 2017;30(4):446–9.
22 Chapelle N, Musquer N, Metivier-Cesbron E, Luet D, Volteau C, Le Rhun M, et al. Efficacy of a three-day training course in endoscopic submucosal dissection using a live porcine model: a prospective evaluation. United European Gastroenterol J. 2018;6(9):1410–6.

23 Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. PLoS Biol. 2020;18(7): e3000410.
24 Hochberger J, Maiss J, Magdeburg B, Cohen J, Hahn EG. Training simulators and education in gastrointestinal endoscopy: current status and perspectives in 2001. Endoscopy. 2001;33(6):541–9.
25 Parra-Blanco A, Arnau MR, Nicolas-Perez D, Gimeno-Garcia AZ, Gonzalez N, Diaz-Acosta JA, et al. Endoscopic submucosal dissection training with pig models in a Western country. World J Gastroenterol. 2010;16(23): 2895–900.
26 Martinek J, Stefanova M, Suchanek S, Zavada F, Svobodova B, Strosova A, et al. Training of different endoscopic skills on ex vivo animal model. Simul Healthc. 2014;9(2):112–9.
27 Herreros de Tejada A. ESD training: a challenging path to excellence. World J Gastrointest Endosc. 2014;6(4):112–20.
28 Bok GH, Cho JY. ESD hands-on course using ex vivo and in vivo models in South Korea. Clin Endosc. 2012;45(4):358–61.
29 Gerson LB, Van Dam J. Technology review: the use of simulators for training in GI endoscopy. Gastrointest Endosc. 2004;60(6):992–1001.
30 Kato M, Gromski M, Jung Y, Chuttani R, Matthes K. The learning curve for endoscopic submucosal dissection in an established experimental setting. Surg Endosc. 2013;27(1): 154–61.
31 Bhatt A, Abe S, Kumaravel A, Parsi MA, Stevens T, Jang S, et al. Video-based supervision for training of endoscopic submucosal dissection. Endoscopy. 2016;48(8):711–6.
32 Pioche M, Rivory J, Nishizawa T, Uraoka T, Touzet S, O'Brien M, et al. Randomized comparative evaluation of endoscopic submucosal dissection self-learning software in France and Japan. Endoscopy. 2016;48(12):1076–83.
33 Pioche M, Rivory J, Aguero-Garcete G, Guillaud O, O'Brien M, Lafon C, et al. New isolated bovine colon model dedicated to colonic ESD hands-on training: development and first evaluation. Surg Endosc. 2015;29(11): 3209–15.
34 Gromski MA, Cohen J, Saito K, Gonzalez JM, Sawhney M, Kang C, et al. Learning colorectal endoscopic submucosal dissection: a prospective learning curve study using a novel ex vivo simulator. Surg Endosc. 2017;31(10): 4231–7.
35 He Y, Fu K, Leung J, Du Y, Wang J, Jin P, et al. Traction with dental floss and endoscopic clip improves trainee success in performing gastric endoscopic submucosal dissection (ESD): a live porcine study (with video). Surg Endosc. 2016;30(7):3138–44.
36 Teoh AY, Chiu PW, Wong SK, Sung JJ, Lau JY, Ng EK. Difficulties and outcomes in starting endoscopic submucosal dissection. Surg Endosc. 2010;24(5):1049–54.
37 Coda S, Trentino P, Antonellis F, Porowska B, Gossetti F, Ruberto F, et al. A Western single-center experience with endoscopic submucosal dissection for early gastrointestinal cancers. Gastric Cancer. 2010;13(4):258–63.

VII. ENDOSCOPIC SUBMUCOSAL DISSECTION TRAINING PATHWAYS AND CLINICAL OUTCOMES

A) TRAINING IN REFERRAL CENTERS

ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): HOW DO WESTERN ENDOSCOPISTS VALUE ANIMAL MODELS?

Küttner-Magalhães R, Pimentel-Nunes P, Araújo-Martins M, Libânio D, Borges-Canha M, Marcos-Pinto R, Koch AD, Dinis-Ribeiro M.

Scand J Gastroenterol. 2021;56(4):492-497. doi: 10.1080/00365521.2021.1879251.

SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY
https://doi.org/10.1080/00365521.2021.1879251

ORIGINAL ARTICLE

Endoscopic submucosal dissection (ESD): how do Western endoscopists value animal models?

Ricardo Küttner-Magalhães[a,b], Pedro Pimentel-Nunes[c,d,e], Miguel Araújo-Martins[e], Diogo Libânio[c,d], Marta Borges-Canha[e,f], Ricardo Marcos-Pinto[a,b,d], Arjun D. Koch[g] and Mário Dinis-Ribeiro[c,d]

[a]Department of Gastroenterology, Santo António Hospital, Porto University Hospital Center, Porto, Portugal; [b]Institute of Biomedical Sciences Abel Salazar, University of Porto, Porto, Portugal; [c]Department of Gastroenterology, Portuguese Oncology Institute of Porto, Porto, Portugal; [d]Department of Community Medicine, Health Information and Decision (MEDCIDS) and CINTESIS, Faculty of Medicine, University of Porto, Porto, Portugal; [e]Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal; [f]Department of Endocrinology, Diabetes and Metabolism, São João University Hospital Center, Porto, Portugal; [g]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

ABSTRACT

Introduction: Endoscopic Submucosal Dissection (ESD)was introduced in the West later than in the East. Our aim was to assess how Western endoscopists performing ESD have been trained and how they value animal models for training.

Material and methods: An online survey regarding training in ESD was sent to Western endoscopists who published articles on advanced resection techniques.

Results: From 279 endoscopists, 58 (21%) completed the questionnaire, of which 50 confirmed performance of clinical ESD. Endoscopists had a median of 15 years of endoscopic experience (IQR 9.75–20.25) and all of them were performing conventional EMR, before starting ESD. Prior to clinical ESD, 74% ($n = 37$) underwent training with *ex vivo* models, 84% ($n = 42$) with live animal models and 92% ($n = 46$) with at least, one of the two models. After starting clinical ESD, as trainers, 52% ($n = 26$) were involved with *ex vivo* and 60% ($n = 30$) with live animal models. Personal usefulness of *ex vivo* and live animal models was rated with a median of 9 (IQR 8–10) and 10 (IQR 8–10), out of 10, respectively. Courses with *ex vivo* and live animal models were considered a prerequisite before clinical practice by 84% ($n = 42$) and 78% ($n = 39$), respectively.

Conclusions: Western endoscopists have extensive endoscopic experience before starting ESD. The majority had pre-clinical training with *ex vivo* and live animal models and more than half are acting as trainers of other endoscopists with these models. Animal models are considered very useful and deemed a prerequisite before clinical practice by the majority of the endoscopists.

ARTICLE HISTORY
Received 18 December 2020
Revised 14 January 2021
Accepted 16 January 2021

KEYWORDS
Endoscopic submucosal dissection (ESD) animal models; gastrointestinal endoscopy; simulation; training

Introduction

Endoscopic submucosal dissection (ESD) was introduced in Japan in the 1990s. The major advantage of this technique is the ability to achieve en-bloc resection irrespective of size of the lesion, allowing for an accurate tumour histopathological evaluation, higher rates R0 resections and lower rates of local recurrence [1–3].

ESD requires high level of expertise and extensive training. Itis time-consuming, has the potential for serious adverse events and proficiency can only be reached after a long learning curve [4]. Taking in consideration the complexity of the procedure, the shortage of experts to supervise clinical ESD practice and the low prevalence of gastric lesions that are usually recommended for early training, the implementation of ESD in Western countries has been relatively slow [5].

Therefore, Western endoscopy societies have recognized the clear need for well-organized comprehensive strategies to establish adequate ESD training curricula [6]. It is suggested that an expert endoscopist aiming to start performing ESD should follow a training program which encompasses acquiring ESD theory knowledge, observing/assisting procedures, practicing on animal models and only then proceeding to clinical practice under supervision by an expert [1,6–8].

Recommendations regarding the minimum background endoscopic experience of the ESD learner have been made [4,6,9,10]. However, it has been suggested that this previous endoscopic experience might be different from Western and Eastern endoscopists but there are no data to confirm this.

Studies on learning pathways in Eastern countries have been published [10,11], but large scale data on real-world training of Western endoscopists are lacking. Different institutions have resorted to distinct training strategies [8,12] and it is crucial to gain insight in the training curricula that have been developed.

This study aimed to assess how Western endoscopists performing ESD were trained, with specific attention to the use of animal models.

CONTACT Ricardo Küttner-Magalhães rkuttner@gmail.com Santo António Hospital, Porto University Hospital Center, Porto 4099-001, Portugal

Material and methods

Study design and participants

In this cross-sectional study, a comprehensive search on PubMed database was conducted to identify Western studies published on advanced resection techniques, between January 2005 and June 2017, using the following search terms: 'endoscopic mucosal resection' (Title) OR 'EMR' (Title) OR 'endoscopic submucosal dissection' (Title) OR 'ESD' (Title).

From 2943 retrieved articles, 467 were recognized as Western in origin and 279 corresponding authors were identified after duplicates removal (Figure 1). They were invited by email to complete an online survey using *Google's Form* (platform by Google USA). Two additional invitations were sent, in case of non-response, within a 3-month period (January to March 2018). All invitees were informed that answers were handled completely anonymous. This study was part of a larger survey concerning ESD practice and implementation [13]. This was not a research conducted on humans, but based on online questionnaires answered by humans. Completing the questionnaire implied the participant's consent and only the ones who wished to do so responded willingly and all had the possibility of not doing it if they wished. For these reasons written informed consent and Institutional Review Board approval were not necessary.

Survey questionnaire

The structured questionnaire contained items on ESD practice and training. We focused on domains specifically related to training, while results concerning ESD practice were addressed in another study [13]. The survey was divided in three domains. The first part was related to pre-clinical ESD practice, namely, endoscopic experience and attendance of training courses. The second part addressed the role of respondents as trainers in animal courses, after starting ESD practice. The third part focused on the perceptions of animal models as learning tools, referring to usefulness of attending animal courses (appreciation reported in a 10-point Likert scale) and requirement of animal training as a prerequisite for clinical practice. Major clinical ESD outcomes were collected according to the European Guidelines definitions [1].

Statistical analysis

Descriptive statistics were determined for all measures according to type of variables. Proportions were reported for dichotomous and ordinal variables. For continuous variables medians (interquartile (IQR) 25–75%) were described.

The IBM Statistical Package for Social Sciences (SPSS Version 23.0.0; SPSS Inc, Chicago, Ill) was used to store and analyze data.

Results

Participants

From 279 corresponding authors, 58 (21%) completed the survey, of which 50 were performing ESD in clinical practice and thus were included in the analysis (Figure 1). Participants responded from Europe ($n = 39$), America ($n = 10$) and Oceania ($n = 1$).

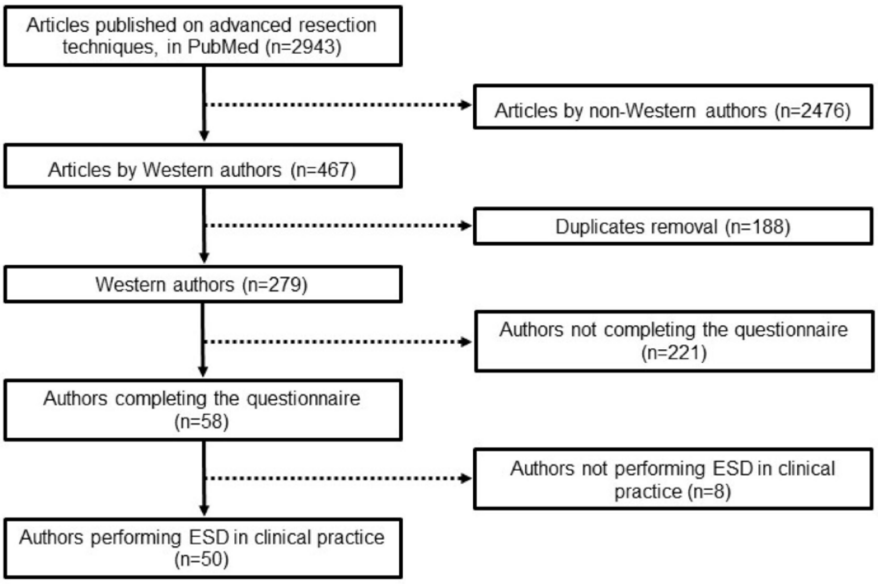

Figure 1. Flow diagram of selection of participants.

Prior experience before clinical ESD practice

Before starting clinical ESD, endoscopists had a median of15 (IQR 9.75–20.25) years of endoscopic experience (Table 1). More than 90% of the respondents were regularly performing upper (n = 46) or lower (n = 48) GI endoscopy and all were performing conventional EMR. About half were performing modified EMR: 56% (n = 28) ligation-assisted EMR and 48% (n = 24) cap-assisted EMR.

Before clinical ESD practice, as ESD trainees, 74% (n = 37) underwent training with *ex vivo* animal models with a median attendance of 2 courses (IQR 1–5) and 84% (n = 42) underwent training with live animal models with a median attendance of 2 courses (IQR 1–4). In 92% (n = 46) at least one of the two models was experienced.

After starting clinical ESD practice

After starting clinical ESD, as trainers, 52% of the respondents (n = 26) were involved in *ex vivo* animal models with a median attendance of 5 courses (IQR 2.75–10) and 60% (n = 30) were involved in live animal models with a median attendance of 3 courses (IQR 2–10) (Table 1).

Animal models as learning tools

When asked to rate how useful it was to attend *ex vivo* animal models courses, before performing human ESD, a median score of 9out of 10 (IQR 8–10) was reached (Table 2). A median score of 10 (IQR 8–10) was attained when referring to live animal models courses.

When asked about the requirement of training in animal models as prerequisite to be allowed to practice clinical ESD, 84% (n = 42) considered to be a prerequisite to attend courses with *ex vivo* models and 78% (n = 39) with live animal models.

Table 1. Data on participants.

Prior to clinical ESD	
Previous endoscopic experience	
Years of endoscopy, median (IQR 25–75)	15 (9.75–20.25)
Regularly performing, *n* (%)	
Upper GI EMR	46 (92)
Lower GI EMR	48 (96)
ERCP	35 (70)
EUS	23 (46)
Inject and cut EMR	50 (100)
Ligation-assisted EMR	28 (56)
Cap-assisted EMR	24 (48)
Courses with animal models, as a trainee	
Ex vivo, *n* (%)	37 (74)
How many: median (IQR 25–75)	2 (1.0–5.0)
Live, *n* (%)	42 (84)
How many: median (IQR 25–75)	2 (1.0–4.0)
Ex vivo or live, *n* (%)	46 (92)
After clinical ESD	
Courses with animal models, as a trainer	
Ex vivo, *n* (%)	26 (52)
How many: median (IQR 25–75)	5 (2.75–10)
Live, *n* (%)	30 (60)
How many: median (IQR 25–75)	3 (2.0–10.0)

EMR: Endoscopic Mucosal Resection; ERCP: Endoscopic Retrograde Cholangiopancreatography; ESD: Endoscopic Submucosal Dissection; EUS: Endoscopic Ultrasonography; GI: Gastrointestinal; IQR: interquartile range.

Major clinical ESD outcomes

According to the type of training in animal models, en bloc, R0 and curative resection rates ranged from 91.9% to 89.0%, 85.1% to 83.9% and 79.8% to 74.9%, respectively (Appendix Table 3). Endoscopists without exposure to animal model training had higher ESD clinical experience, with a mean of 11.5 vs 6, 8 years and more ESD cases per endoscopist (393 vs 230 cases).

Discussion

In this study we describe, for the first time, the worldwide clinical endoscopic experience of Western endoscopists before starting ESD, as well as, their exposure to animal models before and after clinical ESD practice. We concluded that Western endoscopists have extensive endoscopic experience before starting human ESD. The majority had pre-clinical training with *ex vivo* and live animal models and more than half are acting as trainers of other endoscopists with these models. Moreover, animal models are considered very useful and deemed a prerequisite before clinical practice by the majority of the endoscopists.

Concerning the strengths of this study, we stress that it does not represent a single country or continent. Instead there were a very wide range of participating endoscopists from distinct Western countries which contribute to more broader perspectives on this subject and more global conclusions. We can also emphasize that this study explores a crucial, overlooked item which is training, on a demanding technique that still lacks worldwide dissemination.

Regarding the limitations of this study, response rate (21%) was low, although quite reasonable for this type of research. Additionally, since endoscopists performing EMR and not ESD were also invited, many may have felt that it would not be worth answering the questionnaire. Results are based only on endoscopists who published articles on this subject which may reflect more motivated and concerned practitioners even in regard to training. Answers are provided on what respondents recall, as this was not a prospective study, which also limited depth of collected data. Other forms of learning in the training algorithm were not assessed

Table 2. Perspective on usefulness and requirement as prerequisite of training in animal models.

As an ESD trainee, how useful, before clinical practice are courses (from 1–10):	
With *ex vivo* animal models, median (IQR 25–75)	9 (8.0–10.0)
With live animals models, median (IQR 25–75)	10 (8.0–10.0)
Positive opinion that courses should be considered a prerequisite before clinical practice:	
With *ex vivo* animal models, *n* (%)	42 (84)
With live animals models, *n* (%)	39 (78)

ESD: Endoscopic submucosal dissection.

such as, theoretical background, literature, lectures or ESD under supervision. This study represents individual behaviours on this matter and not necessarily integrated endoscopic centres position on training.

ESD is technically challenging so it is advisable that endoscopists considering ESD training should be fully trained and proficient in EMR and adverse event management [6]. In line with the ESGE recommendations on training [6], we verified that, before starting clinical ESD, Western endoscopists are very experienced (median of 15 years of endoscopy) and are all regularly performing EMR. Although not considered absolutely necessary [6] about half practice modified EMR techniques (cap- and ligation-assisted), which provide further experience and knowledge about alternative resection methods.

In Japan a trainee must have 4 to 5 years of endoscopic experience, 1000 upper endoscopies, 100 colonoscopies, 20 therapeutic endoscopies and reliable techniques of hemostasis, polypectomy and endoscopic mucosal resection, before ESD training [4,9,10]. In a Japanese study, learning endoscopists had a mean of 5 years post-graduation and had performed as little as 150–250 colonoscopies [11].

In a Korean survey, 66% of endoscopists starting ESD were second year fellows or have finished the fellowship <5 years and 100% had finished the fellowship <10 years. The majority started the procedure under supervision at their second-year fellowship and have attended more than 50 procedures [14].

So, in fact, we realized that the typical Western ESD learner is quite more endoscopically experienced than the average Eastern counterpart.

The three preferred learning methods, in a study on ESD training in Korea, were ESD under supervision (91%), ESD observation (81%) and hands-on animal courses (35%) [14]. However, the two most important ones are the most difficult to accomplish in the West, due to the shortage of expert endoscopists available to supervise ESD and the lower prevalence of easier located gastric lesions to start performing ESD. To overcome the lack of expert supervision, there are reports of local supervision from Japanese endoscopists in Western countries [15].

Bearing in mind the aforementioned differences between East and West, the typical Eastern ESD training program is not, at least for the time being, a totally reproducible learning pathway in the West. Therefore, a pre-patient training program, incorporating animal model training is recommended [1,6,12,16,17]. Even in Asian countries initial ESD training in humans is not considered appropriate [9] and most experts recommend training with animal models to accelerate the learning curve [10].

Despite some limitations, animal models seem the most adequate to provide training in ESD [18,19]. The porcine model has been considered very realistic compared to the human setting, highly appreciated as a learning tool and has been validated in performing ESD [19]. It has already been demonstrated that through successive animal procedures, complete resections, en bloc resections and ESD speed improve whereas adverse events decrease, supporting the role of animal models in the early learning phase [20,21].

The fact that on our survey the majority of the endoscopists underwent training with animal models underlines compliance with ESGE recommendations [1,6] and Eastern perspectives [9,10] on training and thus recognition of the difficulty and associated risks of the technique.

In Italy, 93% and 76% performed *ex vivo* and *in vivo* ESD training, respectively [22]. In Japan, the number of *ex vivo* or animal training courses needed before starting ESD training in humans is five or less [11]. In Korea, hands-on courses were considered valuable at improving beginners skills at the early phase, although only 33.8% of the endoscopists in one survey, underwent such training [14], which is a much lower percentage than our data on Western endoscopists (84–74%).

Before clinical practice, more endoscopists, in our study, trained on live animal models that on *ex vivo* (84% vs 74%) and this may be related to closer resemblance of this model to the human setting [19]. Live animal models have breathing movements, heart beats, peristalsis, intraluminal secretions, abdominal distension and the possibility of dealing with bleeding and perforation [16,18,19]. Actually, in our study, a large proportion of responding endoscopists that underwent training in animal models are now committed to teaching ESD with these models, which is reflected by the fact that they have now attended more courses as trainers (median of 5 and 3courses with *ex vivo* and live animal model, respectively) that they underwent as trainees (median of 2 courses each with *ex vivo* and live animal model). Obviously, this reveals the high value that they attribute this kind of training.

In line with this relevance was the high scores attributed to the usefulness of attending *ex vivo* and live animal models courses before starting clinical ESD: median of 9 (IQR 8–10) and 10 (IQR 8–10), out of 10, respectively. Also, the majority believed that the attendance such of courses should be a prerequisite before clinical practice.

Expected differences in clinical ESD outcomes would probably occur in the initial clinical practice if an analogy is made with flexible endoscopy simulation-based training [23]. However, this study was not designed for this purpose. Our data refers to total cases, thus, differences in outcomes of endoscopists with different animal model training or non-exposure to these models were not evident. Endoscopists without animal training had higher ESD clinical experience in years and in volume of cases per endoscopist. Therefore, we are reporting more initial outcomes of endoscopists with previous animal training and a more mature experience of endoscopists without animal training. And so, to achieve similar clinical results endoscopists with previous animal training have less years of ESD practice and less ESD cases per endoscopist.

Hence, a structured ESD training program should be implemented including baseline endoscopic experience, theoretical knowledge, observing/assisting ESD procedures, hands-on training in animal models and only then starting clinical procedures, ideally under supervision.

As we disseminate ESD more widely in Western countries the possibility to combine training in animal models with clinical ESD under supervision will perhaps became a reality, but meanwhile these animal courses are of major value to learn ESD.

In conclusion, aligned with the ESGE recommendations [1,6] and Eastern perspectives [9,10] on training, we realize that Western endoscopist's skills and competencies before starting ESD were fulfilled and that the majority had animal training as suggested. These animal models were considered very useful and a prerequisite before clinical practice.

Acknowledgments

We would like to thank all respondents for completing the survey.

Disclosure statement

Ricardo Küttner-Magalhães, Pedro Pimentel-Nunes, Miguel Araújo-Martins. Diogo Libânio, Marta Borges-Canha and Ricardo Marcos-Pinto have no conflicts of interest or financial ties to disclose; Arjun D Koch reports speaker fees from Cook Medical, ERBE, Pentax and Boston Scientific; Mário Dinis-Ribeiro reports research grants from Olympus and Fujifilm.

ORCID

Ricardo Küttner-Magalhães http://orcid.org/0000-0002-8522-5756
Pedro Pimentel-Nunes http://orcid.org/0000-0002-7308-3295
Diogo Libânio http://orcid.org/0000-0003-2691-7522
Mário Dinis-Ribeiro http://orcid.org/0000-0003-0121-6850

References

[1] Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. Endoscopy. 2015;47(9):829–854.

[2] Cao Y, Liao C, Tan A, et al. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. Endoscopy. 2009;41(09):751–757.

[3] Oka S, Tanaka S, Kaneko I, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. Gastrointest Endosc. 2006;64(6):877–883.

[4] Oda I, Odagaki T, Suzuki H, et al. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc. 2012;24(Suppl 1):129–3210.

[5] Pimentel-Nunes P, Mourao F, Veloso N, et al. Long-term follow-up after endoscopic resection of gastric superficial neoplastic lesions in Portugal. Endoscopy. 2014;46(11):933–4010.

[6] Pimentel-Nunes P, Pioche M, Albeniz E, et al. Curriculum for endoscopic submucosal dissection training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2019;51(10):980–9210.

[7] Oyama T, Yahagi N, Ponchon T, et al. How to establish endoscopic submucosal dissection in Western countries. World J Gastroenterol. 2015;21(40):11209–11220.

[8] Friedel D, Stavropoulos SN. Introduction of endoscopic submucosal dissection in the West. World J Gastrointest Endosc. 2018; 10(10):225–238.

[9] Fujishiro M, Jung HY, Goda K, et al. Desirable training and roles of Japanese endoscopists towards the further penetration of endoscopic submucosal dissection in Asia. Dig Endosc. 2012;24 (Suppl 1):121–123.

[10] Goda K, Fujishiro M, Hirasawa K, et al. How to teach and learn endoscopic submucosal dissection for upper gastrointestinal neoplasm in Japan. Dig Endosc. 2012;24(Suppl 1):136–142.

[11] Tsuji Y, Ohata K, Sekiguchi M, et al. An effective training system for endoscopic submucosal dissection of gastric neoplasm. Endoscopy. 2011;43(12):1033–1038.

[12] Kotzev AI, Yang D, Draganov PV. How to master endoscopic submucosal dissection in the USA. Dig Endosc. 2019;31(1):94–10010.

[13] Araujo-Martins M, Pimentel-Nunes P, Libanio D, et al. How is endoscopic submucosal dissection for gastrointestinal lesions being implemented? Results from an International Survey. GE Port J Gastroenterol. 2020;27(1):1–17.

[14] Lee JG, Park CH, Chung H, et al. Current status and trend in training for endoscopic submucosal dissection: a nationwide survey in Korea. PLoS One. 2020;15(5):e0232691.

[15] Yamamoto S, Radomski T, Shafazand M. Implementation of mentor-assisted colorectal endoscopic submucosal dissection in Sweden; learning curve and clinical outcomes. Scand J Gastroenterol. 2018;53(9):1146–1152.

[16] Coman RM, Gotoda T, Draganov PV. Training in endoscopic submucosal dissection. World J Gastrointest Endosc. 2013;5(8): 369–378.

[17] McCarty TR, Aihara H. Current state of education and training for endoscopic submucosal dissection: translating strategy and success to the USA. Dig Endosc. 2020;32(6):851–860.

[18] van der Wiel SE, Kuttner Magalhaes R, Rocha Goncalves CR, et al. Simulator training in gastrointestinal endoscopy - from basic training to advanced endoscopic procedures. Best Pract Res Clin Gastroenterol. 2016;30(3):375–387.

[19] Kuttner-Magalhaes R, Dinis-Ribeiro M, Bruno MJ, et al. Training in endoscopic mucosal resection and endoscopic submucosal dissection: face, content and expert validity of the live porcine model. United Eur Gastroenterol J. 2018;6(4):547–557.

[20] Chapelle N, Musquer N, Metivier-Cesbron E, et al. Efficacy of a three-day training course in endoscopic submucosal dissection using a live porcine model: a prospective evaluation. United Eur Gastroenterol J. 2018;6(9):1410–1416.

[21] Pioche M, Rivory J, Aguero-Garcete G, et al. New isolated bovine colon model dedicated to colonic ESD hands-on training: development and first evaluation. Surg Endosc. 2015;29(11):3209–1510.

[22] Maselli R, Iacopini F, Azzolini F, et al. Endoscopic submucosal dissection: Italian national survey on current practices, training and outcomes. Dig Liver Dis. 2020;52(1):64–7110.

[23] Ekkelenkamp VE, Koch AD, de Man RA, et al. Training and competence assessment in GI endoscopy: a systematic review. Gut. 2016;65(4):607–1510.

Appendix

Table 3. Attendance of courses with animal models, as a trainee and clinical ESD outcomes.

	Attendance of animal model courses			
	Ex vivo	Live	*Ex vivo* or live	None
Endoscopists, *n*	37	42	46	4
Time of ESD practice, years, mean (SD)	7,1 (3,2)	6,7 (3,1)	6,8 (3,1)	11,5 (3,5)
ESD total cases per endoscopist, mean (SD)	252 (297)	229 (282)	230 (275)	393 (475)
ESD total cases, *n*	9326	9621	10573	1570
Esophagus, *n*	1624	1626	1743	340
Gastric, *n*	2829	2939	3504	600
Colorectal, *n*	4873	5056	5326	630
En bloc resection, %	89,0	90,0	89,7	91,9
R0 resection, %	83,9	83,9	84,2	85,1
Curative resection, %	76,2	74,9	75,7	79,8
Intra-procedural perforation, %	3,1	3,1	3,0	1,1
Intra-procedural bleeding, %	1,2	1,1	1,2	0,3
Delayed bleeding, %	4,4	4,5	4,7	2,9
Surgery due to an adverse event, %	1,1	0,8	1,0	0,6

ESD: endoscopic submucosal dissection; SD: standard deviation.

B) TRAINING PATHWAYS AND DEDICATED WORKSHOPS

ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) SKILLS TRANSFER TO CLINICAL PRACTICE AFTER HANDS-ON WORKSHOPS: AN INTERNATIONAL SURVEY.

Küttner-Magalhães R, Dinis-Ribeiro M, Marcos-Pinto R, Rolanda C, Koch AD.

Dig Dis. 2021. doi: 10.1159/000521274.

Digestive Diseases

Endoscopy and Imaging: Research Article

Dig Dis
DOI: 10.1159/000521274

Received: June 24, 2021
Accepted: November 23, 2021
Published online: December 2, 2021

Endoscopic Submucosal Dissection Skills Transfer to Clinical Practice after Hands-On Workshops: An International Survey

Ricardo Küttner-Magalhães[a, b] Mário Dinis-Ribeiro[c, d] Ricardo Marcos-Pinto[a, b, d] Carla Rolanda[e, f, g] Arjun D. Koch[h]

[a]Department of Gastroenterology, Santo António Hospital, Porto University Hospital Center, Porto, Portugal; [b]Institute of Biomedical Sciences Abel Salazar, University of Porto, Porto, Portugal; [c]Department of Gastroenterology, Portuguese Oncology Institute of Porto, Porto, Portugal; [d]Department of Community Medicine, Health Information and Decision (MEDCIDS) and CINTESIS, Faculty of Medicine of Porto, Porto, Portugal; [e]Department of Gastroenterology, Braga Hospital, Braga, Portugal; [f]Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal; [g]ICVS/3B's, PT Government Associate Laboratory, Braga/Guimarães, Portugal; [h]Department of Gastroenterology and Hepatology, Erasmus MC Cancer Institute, University Medical Center, Rotterdam, The Netherlands

Keywords

Endoscopic submucosal dissection · Gastrointestinal endoscopy · Endoscopic skills · Hands-on workshops · Animal models · Simulation · Training

Abstract

Background: Endoscopic submucosal dissection (ESD) is a complex procedure, requiring enhanced technical skills. Translation into clinical practice of ESD training programs has not been documented. Our aim was to assess ESD training pathways of endoscopists participating in dedicated workshops and its clinical impact on ESD outcomes. ***Methods:*** Participants of live porcine models ESD workshops, from 2013 to 2019, were included. They were invited to complete a survey focusing on human ESD performance after training, prior skills/competencies, complete learning pathway, and clinical outcomes. ***Results:*** From 118 invited participants, 40 (34%) completed the questionnaire. Nineteen (47%) endoscopists performed human ESD after the workshop, predominantly male (89%). At the beginning of human ESD, endoscopists had a mean of 7.7 (standard deviation (SD) 4.1) years of endoscopic experience and were all performing endoscopic mucosal resection (and emergency endoscopy. Before ESD practice, 100% of the participants were trained with live animal models and 68% with ex vivo models. The majority started clinical ESD in the lower third of the stomach or rectum (90%), with lesions ≤30 mm (89%). Each endoscopist performed a median of 19 (interquartile range 8–32) cumulative ESDs, over a mean of 3.9 (SD 2.0) years. Total en bloc resection rate was 92%, R0 resection rate 88%, and curative resection rate 86%, whereas adverse events remained <10%. Endoscopists with >10 human ESD procedures achieve clinical competence thresholds. ***Conclusions:*** Participants of ESD workshops are adequately skilled prior to clinical ESD, complying with recommendations for training and properly implementing the technique. Transfer to clinical practice, of prior ESD skills obtained in hands-on training courses, was documented. Structured training programs achieve clinical outcomes exceeding established standards, namely in the very initial clinical phase.

Correspondence to:
Arjun D. Koch, a.d.koch@erasmusmc.nl

Introduction

Gastrointestinal cancers represent a clinical heavy burden worldwide. Esophageal, gastric, and colorectal cancers combined represent 18.7% of total cancer incidence and 22.7% of cancer-related mortality [1]. Technology development as well as related skills and training present an increasing challenge for diagnosis and treatment of these diseases.

Endoscopic submucosal dissection (ESD) is currently used for treating superficial gastrointestinal neoplasms. The advantages over conventional endoscopic mucosal resection (EMR) are the ability of en bloc, R0 resection of lesions >20 mm, lowering the risk of local recurrence and allowing reliable histologic evaluation [2, 3]. When compared to surgical treatment in selected patients, ESD is associated with a lower rate of adverse events, shorter operative and hospitalization time, lower costs, and increased quality of live, with similar oncological outcomes [4, 5].

However, ESD is a complex procedure, requiring enhanced technical skills, carrying considerable risks of adverse events and has a prolonged learning curve [6]. Hence, ESD training programs [3, 7–11] have been developed. These typically include baseline endoscopic experience, theoretical knowledge, observing/assisting ESD procedures, hands-on training in animal models, and starting clinical practice, under the supervision of an expert. Their widespread implementation has been heterogenous [12–14] and clinical benefits have not been demonstrated.

Training in animal models plays an important role in the preclinical early learning phase, leading to an improvement in en bloc resection rates and ESD speed as well as a decrease in adverse events [15, 16]. Nevertheless, translation into clinical practice of a structured training program has not been yet documented. Our aim was to assess ESD training pathways of endoscopists participating in dedicated workshops and its clinical impact on ESD outcomes.

Methods

Study Design and Participants

Participants of EMR and ESD workshops with hands-on training with live porcine models from 2013 to 2019 were invited by email to answer an online survey. The workshops were co-organized by the European Association for Gastroenterology, Endoscopy and Nutrition (EAGEN) as well as the European Society of Gastrointestinal Endoscopy (ESGE) and were supported by a grant from United European Gastroenterology (UEG), to develop the workshop during the first 3 years and make it accessible for endoscopists from all socioeconomic regions in Europe.

The questionnaire was built in Google Forms (Google USA) and sent from July to November 2020 (a maximum of 3 requests, in case of nonresponse). The study protocol was approved by the Institutional Review Board of the Institute of Biomedical Sciences Abel Salazar, University of Porto (Ref No. SD/HCC/79).

Invitees were informed that data would be analyzed and that completing the questionnaire was voluntary. Identity protection and confidentiality of the collected data was guaranteed according to the General Data Protection Regulation. Accordingly and in agreement with the Ethics Committee for Health of the Institute of Biomedical Sciences Abel Salazar, University of Porto, completing the questionnaire implied the participant's implicit acceptance/consent.

Workshops

Workshops had a duration of 2 days and included theoretical lectures and hands-on practice in live porcine models. They were held in the training centers of the Erasmus School of Endoscopy at the Erasmus University Medical Center in Rotterdam, The Netherlands; Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal; and Experimental-Research Center ELPEN, Athens, Greece.

The use of live porcine models for training purposes in the workshop was approved by local Ethical Committees for the welfare of animals in medical training. Procedures were conducted in accordance with the "Animal Research: Reporting of In Vivo Experiments" (ARRIVE) Guidelines [17].

Live pigs (*Sus scrofa domesticus*) weighing between 30 and 40 kg were used. Animals were given a liquid diet for 3 days and fasted for 8 h before the procedures. General anesthesia with endotracheal intubation and mechanical ventilation was performed, according to local protocol, with the support of the veterinarian staff throughout the course.

Fully equipped interventional endoscopy workstations were used under the supervision of international faculty experts. Conventional flexible endoscopes, endoscopic ancillary devices, and electrosurgical units were used. The training modules consisted of esophageal multiband EMR, esophageal ESD, gastric ESD, as well as adverse event management, as previously described [18].

Survey Questionnaire

The questionnaire was divided into 7 parts. Demographic data were initially collected. Then, the participants were inquired if they were performing human ESD after attending the workshops. If they were nott, reasons for that were assessed. Endoscopists practicing clinical ESD (human ESD in the endoscopist's hospital) were asked to continue the survey. Further domains focused on skills/competence prior to starting clinical ESD, training methods employed, clinical ESD performance with outcomes (characterized according to the European Guidelines definitions [3]), and appreciation of the learning pathway (in a 10-point Likert scale).

Statistical Analysis

The IBM® Statistical Package for Social Sciences (SPSS®, Version 26; SPSS Inc, Chicago, IL, USA) software was used to store and analyze data. Descriptive statistics were determined for all measures according to type of variables. For quantitative variables, means (with SD) were described when data assumed a normal distribution according to the Shapiro-Wilk test, Kolmogorov-Smirnov and visual inspection of histograms, and normal Q-Q plots. Otherwise, medians (with interquartile range (IQR) 25–75) were employed. Paramet-

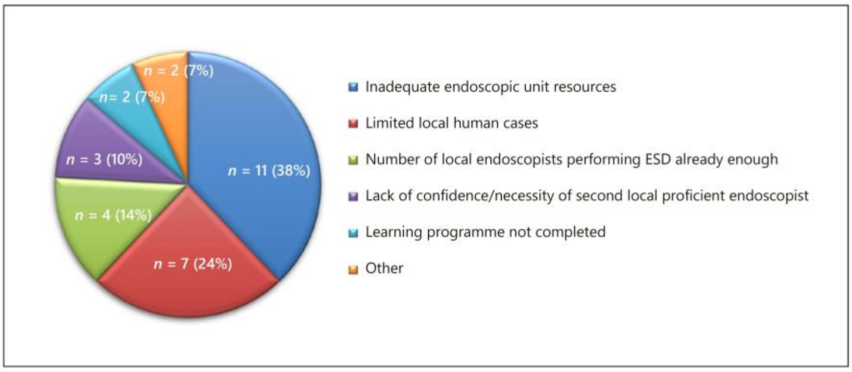

Fig. 1. Reasons for not starting ESD in humans.

Table 1. Participants' characterization

	Global	Performing ESD in humans	Not performing ESD in humans	*p* value
Participants, *n* (%)	40 (100)	19 (47)	21 (53)	
Female (%)	10 (25)	2 (11)	8 (38)	0.044
Age in years, mean (SD)	43.9 (7.7)	43.9 (6.9)	44.0 (8.7)	0.982
Origin, *n* (%)				
Europe	32 (80)	14 (74)	18 (86)	0.307
Asia	5 (12)	2 (10.5)	3 (14)	
South America	2 (5)	2 (10.5)	0	
Oceania	1 (3)	1 (5)	0	
Background formation, *n* (%)				
Gastroenterology	38 (95)	18 (95)	20 (95)	0.942
Surgery	2 (5)	1 (5)	1 (5)	
Working place, *n* (%)				
Academic or tertiary center	26 (65)	15 (79)	11 (52)	0.178
Regional hospital	13 (32)	4 (21)	9 (43)	
Private clinic	1 (3)	0	1 (5)	
Follow-up after workshop, in years, mean (SD)	3.5 (2.3)	3.9 (2.0)	3.2 (2.5)	0.318

ric and nonparametric tests were used to assess statistical differences between groups (*t* test or Mann-Whitney U test). Proportions were reported for categorical variables and comparisons performed with χ^2 test. Significance level was defined as $p < 0.05$.

Results

Participants

From 118 invited participants, 40 (34%) completed the questionnaire. The mean global age was 43.9 (standard deviation [SD] 7.7) years, 75% were male, 95% gastroenterologists, 80% were working in Europe and 65% in academic or tertiary centers (Table 1). The mean follow-up after the workshop was 3.5 (SD 2.3) years. Nineteen (47%) endoscopists performed human ESD after the workshop. From these, there was a predominance of male gender (89%) as well as working in academic or tertiary centers (79%). In total, 20% (2/10) of the female participants started clinical ESD, while 56.7% (17/30) of males did so (p = 0.047). Major reasons not to initiate human ESD were inadequate endoscopic unit resources (38%) and limited local human cases suitable for the technique (24%) (Fig. 1).

Table 2. Skills/competence when starting clinical ESD and training

	n = 19
Familiarity with endoscopic classifications, *n* (%)	19 (100)
Endoscopic experience (after formal residency program)	
Years, mean (SD)	7.7 (4.1)
Performance of	
Upper GI EMR, *n* (%)	19 (100)
Lower GI EMR, *n* (%)	19 (100)
Inject and snare EMR, *n* (%)	19 (100)
Band and snare EMR, *n* (%)	14 (74)
Cap and snare EMR, *n* (%)	12 (63)
Bleeding control (emergency procedures), *n* (%)	19 (100)
ERCP, *n* (%)	11 (58)
EUS, *n* (%)	9 (47)
Before starting clinical ESD	
"ESD theory literature," *n* (%)	18 (95)
ESD meetings, symposiums, conferences, and live demonstrations, *n* (%)	18 (95)
After starting clinical ESD	
ESD meetings, symposiums, conferences, and live demonstrations, *n* (%)	19 (100)
On site observation of human ESD performed by experts, *n* (%)	18 (95)
How many, median (IQR)	3 (1–4)
Assistance in human ESD, *n* (%)	9 (47)
How many, median (IQR)	2 (1–3.5)
Confirmation of knowledge and skills, by an ESD expert, before clinical ESD, *n* (%)	10 (53)
Before starting clinical ESD	
Courses with ex vivo animal models, *n* (%)	13 (68)
How many courses, median (IQR)	2 (1.5–3)
How many ESD procedures (total), median (IQR)	10 (4.5–20)
Supervision by trainers, *n* (%)	13 (100)
Courses with live animal models, *n* (%)	19 (100)
How many courses, median (IQR)	3 (1–4)
How many ESD procedures (total), median (IQR)	10 (5–20)
Supervision by trainers, *n* (%)	19 (100)
After starting clinical ESD	
Courses with ex vivo animal models, *n* (%)	6 (35)
How many, median (IQR)	2 (1–4)
Courses with live animal models, *n* (%)	9 (60)
How many, median (IQR)	1 (1–2.5)
Time from first animal model course to first human ESD, months, median (IQR)	18 (6–36)
Time from last animal model course to first human ESD, months, median (IQR)	3 (1–6)

ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography.

Skills/Competence when Starting Clinical ESD Practice

At the beginning of human ESD practice, endoscopists had a mean of 7.7 (SD 4.1) years of endoscopic experience (after formal residency program; Table 2). All the participants were familiar with and made use of morphologic and chromendoscopic classifications. They were all performing upper and lower GI EMR and endoscopic bleeding control procedures.

Training

Before starting human ESD, 95% had accessed "ESD theory literature" resources (books, articles, DVDs, internet, and including videos) and had attended meetings, symposiums, conferences, and live demonstrations (Table 2). Likewise, 95% had observed, on site, human ESD procedures performed by experts (median of 3 [IQR 1–4]) and 47% had assisted in human ESD procedures by manipulation of endoscopic accessories, patient monitoring, drug administration, etc. (median of 2 [IQR 1–3.5]). Confirmation of knowledge and skills

Table 3. Initial clinical ESD

	n = 19
ESD registration in prospective database, *n* (%)	11 (58)
Possibility of admitting patients to a ward, *n* (%)	19 (100)
Access to emergency surgical team, *n* (%)	19 (100)
Access to expert gastrointestinal pathology, *n* (%)	19 (100)
Supervision of an ESD-proficient endoscopist in first human ESD	10 (53)
How many, *n* (%)	
1–5	7 (70)
6–10	2 (20)
11–20	1 (10)
Organ of first human ESD, *n* (%)	
Esophagus	1 (5)
Middle third of the stomach	1 (5)
Lower third of the stomach	9 (48)
Rectum	8 (42)
Lesion size of first human ESD, *n* (%)	
<20 mm	5 (26)
20–30 mm	12 (63)
>30 mm	2 (11)

Table 4. Clinical ESD outcomes

Organ	Esophageal	Gastric	Rectal	Colonic	Total
Endoscopist ESD experience, *n* (%)	7/19 (37)	17/19 (89)	16/19 (84)	6/19 (32)	19/19
Endoscopist ESD primary organ, *n* (%)	1/19 (5)	9/19 (47)	8/19 (42)	1/19 (5)	–
ESD total number of cases	30	293	147	40	510
ESD total number of cases per endoscopist, median (IQR)	4 (2–5)	10 (4.5–17.5)	5.5 (3.25-12.75)	3.5 (1–10.3)	19 (8–32)
En bloc resection, %	97	97	87	78	92
R0 resection, %	93	92	84	73	88
Curative resection, %	93	89	82	70	86
Surgery due to noncurative resection, %	0	7	5	10	6
Intra-procedural perforation, %	7	3	7	13	5
Intra-procedural bleeding, %	0	0	1	0	<1
Delayed bleeding, %	3	2	4	5	3
Surgery due to an adverse event, %	3	1	0	10	1

by an ESD expert, before starting clinical ESD was possible in 53%.

Prior to clinical ESD, 68% trained with supervised ex vivo animal models, attending a median of 2 (IQR 1.5–3) courses and performing a median of 10 (IQR 4.5–20) ESD procedures in total. Regarding supervised live animal models, attendance of courses was 100%, with a median of 3 (IQR 1–4) courses and 10 (IQR 5–20) ESD procedures in total.

After beginning clinical ESD, 35% continued training with ex vivo animal models, attending a median of 2 (IQR 1–4) courses. Training with live animal models occurred in 60%, with a median of 1 (IQR 1–2.5) course.

Time from first and last animal model course to first human ESD was 18 months (IQR 6–36) and 3 months (IQR 1–6), respectively.

Initial Clinical ESD

Clinical ESD procedures were prospectively registered by 58% of participants (Table 3). All had access to multidisciplinary management of patients.

The first human ESD was performed under the supervision of a proficient endoscopist in 53% and was conducted in the lower third of the stomach or rectum in 90% of cases. The correspondent lesion size was ≤30 mm in 89%.

Clinical ESD Outcomes

More than 80% of participants had experience in gastric or rectal ESD (89% and 84%, respectively), and these were the primary organs for which the technique was used (47% and 42%, respectively; Table 4).

Table 5. Outcomes according to the total number of procedures per endoscopist

Number of ESD procedures per endoscopist	≤10	>10	*p* value	Total
Endoscopists, *n*	6	13		19
ESD total number of cases	32	478		510
ESD total number of cases per endoscopist, median (IQR)	4.5 (3.25–8.50)	30.0 (17.0–41.0)	0.001	19 (8–32)
ESD number of cases per endoscopist/last year, median (IQR)	4.0 (3.75–4.25)	15.0 (10.0–27.0)	0.001	10 (4–24)
En bloc resection, %	84	93	0.0799	92
R0 resection, %	81	89	0.2089	88
Curative resection, %	75	87	0.0684	86
Surgery due to noncurative resection, %	15.6	5	0.0154	6
Intra-procedural perforation, %	6.3	5	0.7876	5
Intra-procedural bleeding, %	0	<1	0.8003	<1
Delayed bleeding, %	0	3	0.297	3
Surgery due to an adverse event, %	0	2	0.4858	1

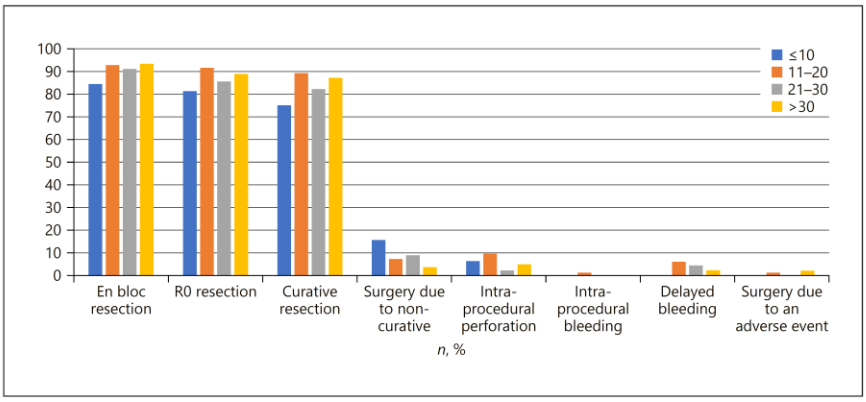

Fig. 2. Outcomes according to the total number of procedures per endoscopist.

Each endoscopist performed a median of 19 (IQR 8–32) cumulative ESDs and a median of 10 (IQR 4–24) ESDs in the last year. Total en bloc resection rate was 92%, R0 resection rate 88%, and curative resection rate 86%, whereas adverse events remained <10%.

A higher number of gastric ESDs were performed (293 in total; median of 10 (IQR 4.5–17.5) per endoscopist) followed by rectal ESDs (147 in total; median of 5.5 (3.25–12.75) per endoscopist).

En bloc resection rates were higher for esophageal (97%) and gastric (97%) lesions and lower for rectal (87%) and colonic lesions (78%). Similarly, R0 resection rates were higher for esophageal and gastric lesions (93% and 92%, respectively) and lower for rectal (84%) and colonic lesions (73%). Also, the curative resection rates were higher for esophageal and gastric lesions (93%, 89%, respectively) and lower for rectal (82%) and colonic lesions (70%).

Regarding adverse events, globally, intra-procedural perforation and bleeding occurred in 5% and <1%, respectively. Delayed bleeding was reported in 3% and surgery due to an adverse event in 1%. These events were more frequent in the colon with 13% of intra-procedural perforation and 10% for surgery due to an adverse event compared to 3% and 1%, respectively, in gastric procedures.

Endoscopists performing ≤10 human achieved en bloc, R0, and curative resection rates of 84%, 81%, and 75%, compared to 93%, 89%, 87%, respectively, for endoscopists with >10 procedures (Table 5). Differences were not statistically significant with the exception of surgery due to noncurative resection (15.6% vs. 5%, $p = 0.0154$).

Table 6. Appreciation of the learning pathway

	n = 19
Satisfaction with training pathway, median (IQR)	7 (7–9)
As an ESD trainee, before clinical ESD practice	
Courses with ex vivo animal models	
Usefulness, median (IQR)	7 (5–10)
Consideration as a prerequisite, *n* (%)	12 (63)
Courses with live animal models	
Usefulness, median (IQR)	10 (9–10)
Consideration as a prerequisite, *n* (%)	17 (89)
Most valuable individual learning methods	
Courses with live animal models	18 (32)
Human ESD under supervision	12 (21)
Observing human ESDs performed by experts	11 (19)
ESD meetings, symposiums, conferences, and live demonstrations	7 (12)
Courses with ex vivo animal models	5 (9)
"ESD theory literature"	4 (7)
Methods lacking for better ESD training	
Centers for observing/assisting human ESDs performed by experts	15 (39)
ESD courses with live animals models	13 (34)
ESD meetings, symposiums, conferences, or live demonstrations	4 (11)
ESD courses with ex vivo animal models	3 (8)
"ESD theory literature"	3 (8)

En bloc, R0, and curative resection rates were above 90%, 85%, and 80%, respectively, for endoscopists performing 11–20, 21–30, and >30 (Fig. 2).

Appreciation of the Learning Pathway

When evaluating the satisfaction with the training pathway of each endoscopist, a median grade of 7 out of 10 (IQR 7–9) was scored (Table 6). The usefulness of courses with ex vivo animal models was appreciated with a grade of 7 (IQR 5–10) and in 63% they were considered to be a prerequisite prior to human ESD. The usefulness of courses with live animal models was rated with a grade of 10 (IQR 9–10) and they were considered to be a prerequisite by 89%.

Courses with live animal models (32%), human ESD under direct supervision (21%) and observing human ESDs performed by experts (19%) were the most valued learning methods. Endoscopists elected centers for observing/assisting human ESDs performed by experts (39%) and additional ESD courses with live animal models (34%) as the main methods lacking for better ESD training.

Discussion

To the best of our knowledge, this is the first study to describe the transfer to clinical practice, of prior ESD skills obtained in hands-on training courses. Furthermore, structured training programs achieve clinical outcomes exceeding established standards, namely, in the very initial clinical phase.

Endoscopists participating in EMR/ESD workshops are adequately skilled prior to human ESD initiation, complying with most of the pre- and post-clinical steps recommended for training and appropriately implementing the technique in clinical practice. Slightly more than half of the included endoscopists (53%) did not start human ESD after attendance of the workshops. We might infer that their training plan was not adequately organized and perhaps not every step of the program was timely arranged. Nevertheless, the majority of the invoked reasons can be locally addressed like adjusting endoscopic unit resources and increasing detection/referral of patients with lesions suitable for ESD.

From the endoscopists that started clinical ESD, most were male endoscopists, as in other reports [12]. Familiarity with endoscopic classifications, prior endoscopic therapeutic skills as well as literature and meetings resources were undertaken, in accordance with main recommendations [3, 9, 19, 20]. We should take into account that, for instance, the recommendations for ESD training by the ESGE [9] were only issued in 2019 and that many endoscopists had already started clinical ESD by that time.

We noted a current trend to decreasing the endoscopic experience when starting ESD compared to previous Western ESD reports (mean of 7.7 years in the current study vs. median of 15 years in an international survey [14]). However, for ESD learning endoscopists, this experience is still not as low as in Japan where, in 1 study, a mean of 5 years of postgraduation was reported [8] and in Korea where 66% were second year fellows or have finished the fellowship <5 years [21].

Animal models are considered an important tool in ESD training [18, 22], and the ESGE recommends performing at least 20 procedures before human practice [9]. Accordingly, in our study, a median of 5 courses and 20 procedures were accomplished before clinical ESD. Of note, courses were always supervised as recommended [9]. In the Western setting, these models are a frequently used resource, as manifested in an Italian survey, in which 93% of endoscopists performing ESD trained with ex vivo and 76% with live animal models [12]. On the other hand, in Korea, only 60% of the endoscopists used animal training [21].

In our study, even after starting human ESD, 60% still used live animal model training. This allows endoscopists with limited initial human cases to maintain continuous exposure to ESD practice, as previously demonstrated [23] and advocated by the ESGE [9]. Such a strategy underlines the importance of assuring additional and ongoing ESD hands-on courses.

Observation/assistance of experts performing ESD and performing the first human procedures with such supervision is usually suggested [3, 9–11]. One of the difficulties in implementing ESD in the West is having local available endoscopists. Nevertheless, in this study, 95% had the opportunity to observe experts and nearly half assisted in human ESD procedures. Also, 53% were able to start human ESD under supervision, in contrast to only 35.5% in an Italian survey [12], but still not universally as in Asian countries [6, 8, 19–21]. As recommended, the first procedures were performed in the lower third of the stomach or rectum in approximately 90% of the cases and none in the colon [3, 9, 19, 20].

The higher number of procedures performed in the stomach and rectum reflect the prevalence of neoplastic lesions in each endoscopist's country but also the intention to work in the safest and most recommended locations in the beginning of the human learning curve.

The number of ESDs performed in the last year (median of 10) is below 25 per year as suggested by the ESGE [9]. This may be explained by the follow-up inferior to 1 year for some endoscopists and because ESD implementation is a progressive, stepwise process. Accordingly, if we consider only endoscopists who performed more than 30 procedures, the median ESD procedures in the last year increase to 24.

Global clinical outcomes in our study, with resection rates of en bloc 92%, R0 88%, and curative 86%, achieved the required thresholds advocated by the ESGE [9] (en bloc >90%, R0 >80–85%, and curative resections >75%). En bloc, R0, and curative resections rates were higher for esophageal (97%, 93%, and 93%, respectively) and gastric lesions (97%, 92%, and 89%, respectively), intermediate for rectal lesions (87%, 84%, and 82%, respectively), and lower for colonic lesions (78%, 73%, and 70%, respectively). Combined colorectal ESD, attained an en bloc resection rate of 85%, R0 of 82%, and curative of 79%. These results are comparable to or better than other Western series [12, 13, 24]. Adverse events were kept under the 10% considered for early competence [10] and below other national reports (29–14%) [13]. The global perforation rate of 5% in our study, although lower than the 18–8% [13] or 6% [12] of other surveys, was superior to the 3% suggested by the ESGE [9], mainly due to colonic ESD.

Beginning ESD training in humans is strongly discouraged [3, 9, 19, 20]. In a study with nonexperienced endoscopists without supervision, the perforation rate was 34% and the en bloc resection rate 52% in the initial human rectal ESD practice (first 25 cases) [25]. In our report, despite of a low median number of rectal ESD procedures per endoscopist of 5.5, the perforation rate was 7% and en bloc resection rate 87%.

En bloc, R0, and curative resection rates (84%, 81%, and 75%, respectively) for endoscopists performing ≤10 human ESDs were below, or at the ESGE-defined competency thresholds [9]. Even so, these outcomes exceed the en bloc resection defined for the early competency (>80%) [10], but of course it is not possible to exclude that the initial procedures were less complex. When we address endoscopists with >10 procedures the en bloc, R0, and curative resection rates of 93%, 89%, 87%, respectively, surpass the established clinical standards [9] and the results of other Western series [12, 13, 24]. Even acknowledging the limitation of number thresholds in endoscopic learning curves [26], assessment of colonoscopy competency is only recommended after 200–300 cases, which represent the average number of procedures to achieve a cecal intubation rate of 90% [27–29]. As a trainee should not be allowed to practice colonoscopy independently before reaching that threshold (besides other criteria), likewise an ESD trainee should have expert supervision at least in the first 10 human procedures, which is in line with the ESGE recommendations [9].

Therefore, applying a structured training program, including animal model simulation, allows an effective and safe initial human learning curve. Major benefits seem to occur in the early clinical practice, as with validated virtual reality simulators for flexible endoscopy [30, 31]. Other sources of evidence that support the relevance of training, such as prospective comparative studies with or without animal model, do not seem appropriate, lacking common sense and ethical reasoning.

In a Korean survey, only 43% of the participants were satisfied with their training program [21], whereas a median of 7 out 10 was the score attributed in our study. Although the preferred ESD learning methods are common, a greater focus is placed on ESD under supervision/ESD observation in the Asian study [21], while in ours, an emphasis was given to training with animal models. On the other hand, endoscopists in our study look for places in which they can observe/assist ESDs that are scarce in Europe due to the limited number of ESD expertise. In this learning pathway, a clear challenge arises regarding narrowing the existing gap between Asian endoscopist's preferences and European endoscopist's desires (which is the opportunity to observe/assist experts performing human ESD and to start human ESD under supervision) and the European ability to provide such training.

Regarding the strengths of this study, we highlight the worldwide origin of the participants which broadens the impact of our results. Additionally, data are related to a continuum period, addressing different modalities of training, the implementation of the technique, and then the initial human learning curve (where the impact of training program may have a greater impact).

Concerning the limitations, we acknowledge the modest number of respondents (but still satisfactory for this type of study), the low number of procedures performed, and the reliance on self-reported data. In the near future, availability of centers for observation/assisting and starting clinical ESD under expert supervision must be addressed as they are considered scarce, relevant, and desired training methods.

In conclusion, participants of ESD workshops are adequately skilled prior to clinical ESD, complying with recommendations for training and properly implementing the technique. Structured training programs achieve clinical outcomes exceeding established standards, namely, in the very initial clinical phase.

Acknowledgments

We would like to thank all respondents for completing the survey.

Statement of Ethics

The use of the live porcine model for training purposes in the workshops was approved by local ethical committees for the welfare of animals in medical training. Procedures were conducted in accordance with the "Animal Research: Reporting of In Vivo Experiments" (ARRIVE) Guidelines. The study protocol was approved by the Institutional Review Board of the Institute of Biomedical Sciences Abel Salazar, University of Porto (Ref No. SD/HCC/79). This was not a research conducted on humans (but based on online questionnaires answered by humans). Only the ones who wished to do so responded willingly and all had the possibility of not doing it if they wished. Invitees were informed that data would be analyzed and that completing the questionnaire was voluntary. Identity protection and confidentiality of the collected data was guaranteed according to the General Data Protection Regulation. Accordingly and in agreement with the Ethics Committee for Health of the Institute of Biomedical Sciences Abel Salazar, University of Porto, completing the questionnaire implied the participant's implicit acceptance/consent. Therefore, the requirement for written informed consent was waived.

Conflict of Interest Statement

Ricardo Küttner-Magalhães, Ricardo Marcos-Pinto, and Carla Rolanda have no conflicts of interest or financial ties to disclose; Mário Dinis-Ribeiro reports research grants from Olympus and Fujifilm and Medtronic consultancy; and Arjun D. Koch reports speaker fees from Cook Medical, ERBE, Pentax, and Boston Scientific.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial or nonprofit sectors. The workshops were unrestrictedly sponsored by Pentax® (Tokyo, Japan), ERBE® (Tübingen, Germany), Karl Storz (Tuttlingen, Germany) and, Cook Medical® (Winston-Salem, NC, USA), which provided flexible endoscopes, electrosurgical units, and endoscopic devices. The sponsors had no influence on the scientific content of the workshop neither on this study.

Author Contributions

All authors have contributed and agreed on the content of the manuscript. Ricardo Küttner-Magalhães contributed to the study conception, study design, data acquisition, data analysis, data interpretation, manuscript writing, and critical revision. Mário Dinis-Ribeiro contributed to the study conception, study design, study supervision, data analysis, data interpretation, and critical revision of the manuscript. Ricardo Marcos-Pinto and Carla Rolanda contributed to the study conception and design, data interpretation, and critical revision of the manuscript. Arjun D. Koch contributed to the study conception and design, study supervision, data analysis, data interpretation, and critical revision of the manuscript. All authors read and approved the final version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
2 Cao Y, Liao C, Tan A, Gao Y, Mo Z, Gao F. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. Endoscopy. 2009;41(9):751–7.
3 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(9):829–54.
4 Liu Q, Ding L, Qiu X, Meng F. Updated evaluation of endoscopic submucosal dissection versus surgery for early gastric cancer: a systematic review and meta-analysis. Int J Surg. 2020;73:28–41.
5 Libânio D, Braga V, Ferraz S, Castro R, Lage J, Pita I, et al. Prospective comparative study of endoscopic submucosal dissection and gastrectomy for early neoplastic lesions including patients' perspectives. Endoscopy. 2019;51(1):30–9.
6 Oda I, Odagaki T, Suzuki H, Nonaka S, Yoshinaga S. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc. 2012;24(Suppl 1):129–32.
7 Yamamoto S, Uedo N, Ishihara R, Kajimoto N, Ogiyama H, Fukushima Y, et al. Endoscopic submucosal dissection for early gastric cancer performed by supervised residents: assessment of feasibility and learning curve. Endoscopy. 2009;41(11):923–8.
8 Tsuji Y, Ohata K, Sekiguchi M, Ito T, Chiba H, Gunji T, et al. An effective training system for endoscopic submucosal dissection of gastric neoplasm. Endoscopy. 2011;43(12):1033–8.
9 Pimentel-Nunes P, Pioche M, Albéniz 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(10):980–92.
10 Oyama T, Yahagi N, Ponchon T, Kiesslich T, Berr F. How to establish endoscopic submucosal dissection in Western countries. World J Gastroenterol. 2015;21(40):11209–20.
11 Friedel D, Stavropoulos SN. Introduction of endoscopic submucosal dissection in the West. World J Gastrointest Endosc. 2018;10(10):225–38.
12 Maselli R, Iacopini F, Azzolini F, Petruzziello L, Manno M, De Luca L, et al. Endoscopic submucosal dissection: Italian national survey on current practices, training and outcomes. Dig Liver Dis. 2020;52(1):64–71.
13 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(1):45–53.
14 Küttner-Magalhães R, Pimentel-Nunes P, Araújo-Martins M, Libânio D, Borges-Canha M, Marcos-Pinto R, Koch AD, et al. Endoscopic submucosal dissection (ESD): how do Western endoscopists value animal models? Scand J Gastroenterol. 2021;56:1–5.
15 Chapelle N, Musquer N, Métivier-Cesbron E, Luet D, Volteau C, Le Rhun M, et al. Efficacy of a three-day training course in endoscopic submucosal dissection using a live porcine model: a prospective evaluation. United European Gastroenterol J. 2018;6(9):1410–6.
16 Kato M, Gromski M, Jung Y, Chuttani R, Matthes K. The learning curve for endoscopic submucosal dissection in an established experiment setting. Surg Endosc. 2013;27(1):154–61.
17 Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. PLoS Biol. 2020;18(7):e3000410.
18 Kuttner-Magalhaes R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD. Training in endoscopic mucosal resection and endoscopic submucosal dissection: face, content and expert validity of the live porcine model. United European Gastroenterol J. 2018;6(4):547–57.
19 Fujishiro M, Jung HY, Goda K, Hirasawa K, Kakushima N, Lee IL, et al. Desirable training and roles of Japanese endoscopists towards the further penetration of endoscopic submucosal dissection in Asia. Dig Endosc. 2012;24(Suppl 1):121–3.
20 Goda K, Fujishiro M, Hirasawa K, Kakushima N, Morita Y, Oda I, et al. How to teach and learn endoscopic submucosal dissection for upper gastrointestinal neoplasm in Japan. Dig Endosc. 2012;24(Suppl 1):136–42.
21 Lee JG, Park CH, Chung H, Park JC, Kim DH, Lee BI, et al. Current status and trend in training for endoscopic submucosal dissection: a nationwide survey in Korea. PLoS One. 2020;15(5):e0232691.
22 van der Wiel SE, Küttner Magalhães R, Rocha Gonçalves CR, Dinis-Ribeiro M, Bruno MJ, Koch AD. Simulator training in gastrointestinal endoscopy: from basic training to advanced endoscopic procedures. Best Pract Res Clin Gastroenterol. 2016;30(3):375–87.
23 Jacques J, Legros R, Charissoux A, Mesturoux L, Couquet CY, Carrier P, et al. A local structured training program with live pigs allows performing ESD along the gastrointestinal tract with results close to those of Japanese experts. Dig Liver Dis. 2016;48(12):1457–62.
24 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(23):2518–36.
25 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(8):670–6.
26 Yang D, Wagh MS, Draganov PV. The status of training in new technologies in advanced endoscopy: from defining competence to credentialing and privileging. Gastrointest Endosc. 2020;92(5):1016–25.
27 Koch AD, Haringsma J, Schoon EJ, de Man RA, Kuipers EJ. Competence measurement during colonoscopy training: the use of self-assessment of performance measures. Am J Gastroenterol. 2012;107(7):971–5.
28 ASGE Standards of Practice Committee; Faulx AL, Lightdale JR, Acosta RD, Agrawal D, Bruining DH, et al. Guidelines for privileging, credentialing, and proctoring to perform GI endoscopy. Gastrointest Endosc. 2017;85(2):273–81.
29 Siau K, Green JT, Hawkes ND, Broughton R, Feeney M, Dunckley P, et al. Impact of the Joint Advisory Group on gastrointestinal endoscopy (JAG) on endoscopy services in the UK and beyond. Frontline Gastroenterol. 2019;10(2):93–106.
30 Ekkelenkamp VE, Koch AD, de Man RA, Kuipers EJ. Training and competence assessment in GI endoscopy: a systematic review. Gut. 2016;65(4):607–15.
31 Koch AD, Ekkelenkamp VE, Haringsma J, Schoon EJ, de Man RA, Kuipers EJ. Simulated colonoscopy training leads to improved performance during patient-based assessment. Gastrointest Endosc. 2015;81(3):630–6.

VIII. Discussion

DISCUSSION

GENERAL CONSIDERATIONS

Endoscopic resection techniques, namely EMR and particularly ESD are complex procedures, requiring advanced skills and involving substantial risk of adverse events. To address these challenges, structured ESD training programs have been proposed. Nevertheless, evidence supporting which distinct steps should be included and how they would translate into benefits for clinical practice have not been documented.

In this section, the results of the manuscripts are comprehensively discussed with the purpose of answering each aim proposed in the thesis.

In our studies we explored the simulation stage of training programs and presented its role in endoscopic procedures, particularly in the live animal model setting.[365] Both the validity and an early learning curve were established for EMR and ESD training with these models.[366, 367] We also determined how expert endoscopists acquired their training in these techniques.[368] Additionally, we assessed how participants of ESD workshops complied with recommendations for training and adequately implemented the technique. Finally, we evaluated how skills obtained in these training courses were transferred to clinical practice.[369]

SIMULATION IN GASTROINTESTINAL ENDOSCOPY TRAINING

THE ROLE OF SIMULATION

Simulation-based training has gained relevance and acceptance in diverse clinical domains, including emergency medicine, anesthesia, obstetrics, neonatal, pediatric and adult critical care.[370-373]

It is widely accepted that allowing untrained or minimally trained clinicians to develop initial practice on patients poses an unacceptable risk, when simulators are available.[374, 375] Simulation in advanced endoscopic techniques fulfils various prerequisites of paramount importance for simulation in medical education.[376, 377] The first is *patient safety*. Simulating novel, infrequent, potential harmful interventions or novel equipment, instead of practicing on real patients is clearly an example of ESD procedures. Other inherent advantages of simulation are the ability for both *skills training* and *competency assessment*. In fact, routine learning and rehearsal of endoscopic skills, as well as practicing management of serious adverse events represent the core of ESD simulation. The field of competency assessment is still a matter for future development. Finally, *improving clinical teaching constraints* is a reason to adopt simulation in general, that undoubtedly relates to ESD teaching. Increasing or replacing medical rotations when clinical sites are limited, while ensuring predictable and reliable clinical experiences justifies resorting to simulation in Medicine overall.[321, 322, 325, 378] In this regard, considering the particular case of ESD teaching, the scarceness of experts and training centers, as well as the paucity of easier and safer located lesions to start performing clinical ESD support the crucial role of endoscopic simulation.

Several disadvantages have been recognized in the traditional mentor-apprenticeship model of learning endoscopy. Those can relate to the patient, to the tutor, to the learner and to the health care structure, as previously discussed.[25, 328, 329, 365] Endoscopic simulators create a low-risk, stress-free, controlled environment, while offering the possibility of teaching technical, non-technical, and cognitive skills.[25, 330-332] Novices or experts may initiate a new procedure or practice a specific new skill, avoiding human patients involvement in the initial part of the learning curve, where potential risks are greater.[365] These features are particularly relevant for ESD learning.

Pure mechanical simulators and virtual reality simulators are inadequate for ESD training due to the absence of characteristics needed to mimic human tissue.[26, 333-337]

Considering its perceived human resemblance, training with animal models prior to human practice has been recommended, although evidence on clinical benefits of such exposure have been lacking until now.

ANIMAL MODEL SIMULATION FOR ADVANCED ENDOSCOPIC RESECTION TECHNIQUES

VALIDATION OF THE MODEL

Animal model simulation allows the training of team coordination with the assistant, understanding devices/electrosurgical units, as well as rehearsing fine movement control of the scope.[15, 16]

Ex vivo models combine a plastic casing with explanted animal organs. They have the advantage of allowing the execution of various therapeutic endoscopic procedures in different organs, such as the esophagus, stomach and colon, with real accessories, in a more realistic environment and with lower costs. On the other side, there are limitations to the number of training procedures per platform, there is a prolonged preparation time and a loss of tissue characteristics compared to human ones is recognized.[12, 19, 379, 380]

Live animal models, generally anesthetized pigs (although others may be used) are considered more realistic, by including real-feel elements, such as breathing movements, heart beats, peristalsis, abdominal distension, intraluminal secretions and tissue reaction to injection and electrocautery.[13, 365, 381] Furthermore these models allow for the possibility of dealing with bleedings and perforations.[12, 365, 366] On the downside, the availability of animals and the need to sacrifice them, the infrastructures and complex equipment requirements, the veterinarian support, ethical concerns and costs, together represent the disadvantages of these models.[12, 16, 18-20]

Ex vivo models are probably adequate for the initial training period considering these constraints.[12, 16, 18-20, 365, 366, 379, 380] The increased similarity of live animal models with the human scenario renders their use more suitable for the subsequent stage of training.

Formal validation of the live porcine model regarding face, expert and content validity, in training EMR and ESD was achieved in our study, by 91 endoscopists participating in 4 workshops.[366]

ESD training programs include hands-on practicing in live animal models and previous papers have focused on ESD feasibility on such models.[5, 12, 13, 27, 28, 365] However, their validation have not yet been formally demonstrated. Considering the acknowledged similarity with human anatomy, practicing advanced endoscopic resection skills in these models seems rational. Nevertheless, for every method, technology or teaching tool, validity evidence should be obtained prior to its effectiveness assessment or financial justification. In addition, an important consideration when using this particular model is the necessity of animal sacrifice. Similarly, demonstration that a simulator is realistic before concluding about its usefulness as a training tool or prior to testing its abilities as an assessment instrument is required.

The validation process encompasses several phases. Face validity relates to the degree to which the model appears to reflect the intended purpose, while content validity refers to the extent to which the relevant, appropriate, comprehensive and consistent contents or domains are incorporated. Expert validity is recognized when the appreciation is performed by experts on the field.[382-384]

Our data seemed robust, once the validation was performed by trainees with previous experience in diagnostic and therapeutic endoscopy and tutors with inherent vast expertise. Furthermore, appraisals by both groups were very similar.

We were able to demonstrate that the model was very realistic with median global classifications ranging between 7,0-8,0 (IQR 5,0-9,0).

When addressing specifically the characteristics of the live porcine model, its major advantages over pure mechanical simulators and virtual reality simulators were confirmed and reflected by the high rates on the ability to reproduce human elasticity, tissue properties and tactile feedback.[334] On the other hand, orientation of organs, thickness and stiffness of the mucosal layer have not been considered so similar.[20, 385] Accordingly, in our study, wall structure of the organ, mucosal thickness and tissue pliability scored the lowest mean values (although medians were comparable). Another study suggested that the porcine mucosal layer was thinner in the proximal stomach and that the thicker distal greater curvature was less adequate for ESD training.[386]

Besides the high scores for realism, the performance of the procedures itself was considered very similar to the human practice. Procedures were seen as accurately resembling human cases, with median scores of 9,0 (IQR 8,0-9,0) for esophageal multiband EMR, 8,5 (IQR 8,0-9,0) for esophageal ESD and 9,0 (IQR 8,0-10,0) for gastric ESD.

We feel that there are some differences between the porcine and the human esophagus wall structure. In workshops, when performing esophageal multiband EMR, contrasting to human practice, it is easier to create a full thickness pseudopolyp resulting in perforation. Accordingly, in our study, the ability to apply the band ligation and to cut the pseudopolyp, was slightly lower rated compared to the other steps in this technique. Similarly, esophageal ESD had lower overall scores concerning how procedures were performed and regarding the coordination of tasks.

Controlling hemorrhage during submucosal dissection has been regarded as one of the most decisive steps in the ESD teaching process.[387] Importantly, the ratings on complication detection and management, namely dealing with hemorrhages, in our study, were very high, with a score of 9,0 (IQR 8,5-9,8 and 8,0-9,7). As a result, we demonstrated that the live porcine model is useful for training all the steps involved in EMR/ESD and equally for intraprocedural complication management. The difficulty of the procedures and the usefulness of live animal simulated procedures also attained high ratings.

Thus, the animal model was highly appreciated as a learning tool reaching median scores of 9,0 (IQR 7,0-10,0) considering how procedures were performed and 9,0-9,5 (IQR 8,0-10,0) for usefulness to beginners.

In line with international recommendations on training, participants considered that live animal courses should be a prerequisite before clinical practice.[5, 214, 233, 240]

It is important to notice that this work did not address the effects of training in the animal model regarding the outcomes in clinical practice.

LEARNING CURVE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION

The validation of the live animal model for EMR and ESD training by itself, does not translate into a potential benefit of its use. Taking this concern into account, in a subsequent study, we assessed ESD performance parameters in 70 procedures carried out by 17 trainees, in the live porcine model. The percentage of complete resections increased from 88,2% to 100%, en bloc resections from 76,5% to 100% and ESD speed from 8,6 to 31,4mm^2/min, from the first to the final procedures.

We were able to demonstrate that through successive ESD procedures in a porcine model, within a hands-on training program, en bloc resection rates and ESD speed increased whereas adverse events decreased.

Improvement in ESD performance on ex vivo animal models has been demonstrated.[16, 338, 339] Variations in ESD progress were noted between studies, animals (porcine or bovine) and organs (esophagus, stomach or colon). On ex vivo colonic models, an inflexion of the learning curve was observed at the 9th ESD procedure, while an ESD goal was only achieved at the 30th procedure by 84% to 50% of trainees, in another study.[339, 341] Others have shown that to achieve a predefined level of competence, 23-25 ex vivo gastric procedures were needed and 30 gastric ESDs led to decreased procedure times, a lower perforation rate and improvement in en bloc resection rate.[338, 340]

In contrast to other studies, as a more reliable parameter, we chose to use ESD speed instead of surface area or time alone. We realize that an increase in speed (measured in mm^2/min) more accurately reflects ESD performance and the learning curve of the trainee. The isolated use of procedure time or surface area is a weak measure of performance because these parameters are closely related to each other. Hence, at the same speed, more time is necessary to resect a larger lesion and vice versa.

We observed an increase in ESD speed throughout the procedures and importantly, the rate of adverse events did not increase when trainees started performing faster ESDs. On the contrary, the number of procedures in which a trainee needed tutor intervention and the number of adverse events decreased throughout the procedures (4 to 0 and 6 to 0, respectively), as performance and speed improved, reflecting adequate acquisition of skills.

In live models studies, with en bloc resection rates ranging from 94,7 to100%, mean ESD speed varied from 5,0-10,0mm^2/min in the first procedures to 22,0-30,0mm^2/min in the later ones.[388-390] This is in line with our results, in which speed ranged from a median of 8,6mm^2/min in the first procedures to 24,7mm^2/min and 31,4mm^2/min in the final ones.

A temporary decrease in ESD speed (18,5mm^2/min to 17,0mm^2/min) and a slight increase in perforation rate (0 to 2) occurred when trainees switched to a different type of knife. At this point, complete and en bloc resection rates were not affected. ESD performance was gradually improving and had a momentary negative impact by the introduction of a new type of knife. So, we concluded that each endoscopist needs to get used to a certain type of knife and changing it leads to an adaptive phase. Interestingly, this phenomenon happened despite the introduction of a theoretically “safer” knife due to its partial insulated tip. This evidence supports one informal advice, usually provided by ESD experts, which is not to switch repeatedly the type of knife used in clinical practice and to maintain experience with the same one.

Concerning adverse events, the perforation rate was 10,0%, reflecting ESD difficulty, but still in accordance with other studies, with rates of 5,2 to 62,5%for live animal models and 4,6 to 14,5% for ex vivo models.[338-341, 389-392]

In our study we did not observe a plateau phase, which is probably explained by the limited number of ESD procedures performed by each endoscopist with a median of 4,0 (IQR, 3,5-5,0). This confirms the need and rationale for continuous training, even though, as seen in previous studies, assessing ESD learning curves on animal models depends on the type of animal, ex or in vivo nature, definitions of success and competency thresholds assumed. Nevertheless, a minimum of 10 to 30 ESD procedures in the animal model are recommended before moving to human cases.[5, 14, 340, 342]

STRENGTHS AND LIMITATIONS

Concerning the strengths of these studies, we emphasize that the first was a pioneer research and the second had a prospective design, in which the measured parameters were clearly objective and were assessed by an independent observer. In both, endoscopists had diverse origins and backgrounds, which supports the generalization of our findings.

Regarding limitations, it is important to mention that only esophageal and gastric procedures were performed and the porcine colon was not evaluated. We recognize that, in clinical practice, target lesions for ESD may contain fibrosis or involve the submucosal layer which may interfere with endoscopic dissection. In our studies, procedures were performed on healthy porcine tissue with no pathological findings. Nonetheless, the basic steps and strategies will be unaffected in a significant number of such lesions. This known limitation of this model should not be particularly relevant for the beginners in ESD (for whom this training is best suited), because they should not start clinical practice with lesions with such demanding characteristics.

ENDOSCOPIC SUBMUCOSAL DISSECTION TRAINING PATHWAYS AND CLINICAL OUTCOMES

TRAINING IN REFERRAL CENTERS

In a forward stage of the training pathway, we assessed the exposure to training with animal models and the clinical endoscopic background of Western endoscopists performing clinical ESD. From a total of 279 invited expert endoscopists performing advanced resection techniques, 58 (21%) participated and 50 were conducting clinical ESD. They had extensive endoscopic experience before starting human ESD. The majority had pre-clinical training with ex vivo and live animal models and were currently training other endoscopists with these models.

ESGE recommendations on training suggest that endoscopists considering ESD should be fully trained and proficient in EMR and adverse event management.[232] In this study we demonstrated that Western endoscopists were very experienced, with a median of 15 years (IQR 9,8-20,3) of endoscopic exposure and all of them were regularly performing conventional EMR, before starting ESD. Approximately half of them practiced modified EMR techniques (cap- and ligation-assisted EMR), which even though are not deemed absolutely necessary, provide further experience and knowledge about alternative resection methods.[232]

ESD has gained widespread acceptance in the East, where the technique is typically introduced in earlier stages of endoscopic practice. We realized that our typical Western ESD apprentice is fairly more endoscopically experienced than the average Eastern counterpart. Before ESD training in Japan, a trainee is required to have 4 to 5 years of endoscopic experience, 1000 upper endoscopies, 100 colonoscopies, 20 therapeutic endoscopies and reliable techniques of hemostasis, polypectomy and endoscopic mucosal resection.[7, 241, 393] So, for instance, a Japanese study revealed that endoscopists learning ESD had a mean of 5 years of post-graduation and had performed a modest number of colonoscopies (150-250).[239] Similarly, in another survey, 100% of endoscopists starting ESD in Korea, had finished the fellowship <10 years and 66% were second year fellows or have finished the fellowship <5 years.[394]

Concerning the learning process, still in Korea, the three most valued methods were ESD under supervision (91%), ESD observation (81%) and hands-on animal courses (35%).[394] Importantly, the two most significant ones are the most challenging to achieve in the West, due to the lack of endoscopists available to perform and supervise ESD and also due to the low prevalence of antral gastric lesions adequate to initiate human ESD. Local guidance from Japanese endoscopists in Western countries have been reported in an effort to overcome the lack of expert supervision.[395]

The classic Eastern ESD learning pathway is not, currently, entirely reproducible in the West, if we consider the previous mentioned differences between regions. So, a pre-clinical training program incorporating animal model training plays a crucial, irreplaceable role.[5, 12, 232, 364, 396] Even in Asian countries it is not considered appropriate to start ESD in humans and training with animal models is recommended by experts.[241, 393]

As a result, and in compliance with the ESGE recommendations and Eastern perspectives on training, in our survey 84% of the endoscopists underwent training with live animal models, 74% with ex vivo models, and 92% with at least, one of the two models.[5, 232, 241, 393] Similarly, in an Italian study, 93% of learning endoscopists performed ex vivo and 76% in vivo ESD training.[29] On the other hand, in Japan, it is required to attend five or less animal training courses before starting human ESD.[239] Whereas in Korea, despite considered valuable at improving beginners skills at the early phase, only 33,8% of the endoscopists underwent hands-on courses, in one survey.[394] These findings represent a much lower percentage of animal training, when compared to the 92% of Western endoscopists.

Interestingly, in our study, prior to clinical practice, more endoscopists used live animal models than ex vivo models (84% vs 74%), which may be explained by the closer similarity of this model to the human setting.[366]

We realized that, after starting clinical ESD, 60% of the endoscopists became tutors with live animal models and 52% with ex vivo models. In fact, they have attended more courses as trainers (median of 5 courses with ex vivo and 3 courses with live animal models) that they experienced as trainees (median of 2 courses each, with ex vivo and live animal models). We can assume that this teaching method is highly valued, since so many endoscopists that underwent such training later engaged in teaching with the same model.

Accordingly, these endoscopists rated the personal usefulness, before starting clinical ESD, of ex vivo models with a median of 9,0 (IQR 8,0-10,0) and of live animal models with a median of 10,0 (IQR 8,0-10,0), out of 10. They also considered that courses with ex vivo (by 84%) and live animal models (by 78%) should be a prerequisite before clinical practice.

Major clinical ESD outcomes were similar between endoscopists with or without previous animal model training. However, these later endoscopists had greater ESD experience with a mean of 11,5 years (vs 6,8 years) and had performed more ESD cases with a mean of 393 cases (vs 230 cases). The fact is that we would expect that differences in clinical results would manifest in the initial human practice, if we made an analogy with flexible endoscopy simulation-based training.[26] Although the design of this study was not intended for this purpose and taking into account some interpretation caution, we can assume that to achieve similar clinical outcomes, endoscopists with previous animal training have less ESD clinical experience in years and in volume of cases per endoscopist.

TRAINING PATHWAYS AND DEDICATED WORKSHOPS

We conducted a subsequent research, in which we described the transfer of prior ESD skills obtained in hands-on training courses to clinical practice. From the 118 invited endoscopists attending ESD workshops with live porcine models, 40 (34%) participated in our survey and 19 (47%) were performing human ESD thereafter.

The ones that did not start human ESD stated, mostly, local potential addressable justifications such as insufficient detection/referral of patients with lesions suitable for ESD and inadequate endoscopic unit resources.

Endoscopists performing human ESD were predominantly male (89%), as observed in other reports.[29] In accordance with international recommendations, at the beginning of human ESD practice, they had access to literature/meetings resources, were familiar with endoscopic classifications and had acquired adequate endoscopic skills (they were all performing EMR and emergency therapeutic endoscopy).[5, 232, 241, 393]

Interestingly, the mean years of endoscopic practice was 7,7 (SD 4,1) compared to a median of 15 years in our previous Western research, denoting a tendency to a decrease in the endoscopic experience, when starting ESD.[368] Nevertheless, not as low as the experience reported in Asian countries.[7, 239, 241, 393, 394] This means that ESD is gradually disseminating and being implemented in Western countries by younger endoscopists.

In 2019, ESGE released recommendations for ESD training, although many endoscopists in our study had already started clinical ESD by that time.[232] ESGE suggested training with animal models and recommended at least 20 procedures before human practice.[232] In our survey, before human ESD, 100% of the endoscopists used live animal models and 68% ex vivo models, attending a median of 5 courses and performing a median of 20 procedures. As recommended, these courses were always supervised.[232] Animal models are a commonly used training method in the West and less frequent in the East, as previously mentioned.[29, 394]

Endoscopists with few initial human cases, should maintain uninterrupted practice of ESD with animal models.[232, 397] Accordingly, we realized that even after starting clinical ESD, 60% continued using live animal model training. So, efforts should be made to assure continuous availability of additional ESD hands-on workshops.

The scarcity of expert endoscopists to allow observation, assistance and ESD performance under guidance represent one of the challenges, when implementing the technique in the West. Regarded as important training stages, in our study, observation of experts was possible in 95%, assistance in almost 50% and initiating ESD under supervision in 53%.[5, 13, 232, 343] This last step, although not as widespread as in Asian countries, was higher than the 35,5% of an Italian study.[7, 29, 239, 241, 393, 394]

The first clinical procedures were conducted in the lower third of the stomach or rectum (none in the colon), with lesions with ≤30mm, in approximately 90% of the cases, as generally recommended.[5, 232, 241, 393] The stomach and rectum were the locations where the majority of the procedures were performed, where more than 80% of participants had experience and represented the primary organs for ESD in approximately 90% of the cases. We believe that this predominance reflects the prevalence, identification and referral of such lesions in each endoscopist country, as well as the conscious will to work in the easiest and safest locations, in the beginning of human practice.

ESGE recommends a minimum case load of 25 ESDs per year.[232] In our study, we realize that each endoscopist performed a median of 19 (IQR 8-32) cumulative ESDs in total and a median of 10 (IQR 4-24) in the previous year. These numbers are below the suggested threshold, although we should take into account that the implementation of the technique is gradually progressive and that the follow up time for some participants was less than 1 year. Thus, in the previous year, the median procedures increased to 15 (10-27) and 24 (IQR 22-35), if only endoscopists performing more than 10 and 30 procedures were considered, respectively.

Clinical outcomes regarding en bloc, radical (R0) and curative resection rates were, respectively, 92%, 88% and 86%, which exceed the ESGE requirements of >90%, >80%-85% and >75%.[5, 232] These rates were better for esophageal and gastric ESD, intermediate for rectal ESD and lower for isolated colonic ESD.

The adverse event rate was <10%, which has been deemed as the threshold for early competence and inferior to 14% to 29% reported in national series.[13, 30] Particularly concerning the perforation rate, ESGE suggests a limit of 3%.[232] Our global rate reached 5% and was mainly related to colonic perforation, but was still inferior to the 18% to 8%-6% of other studies.[29, 30] Altogether these results are analogous or slightly superior to other Western reports and substantially better than the en bloc resection rate of 52% and the perforation rate of 34% described in the first ESD cases performed by endoscopists without prior experience or supervision in another study.[29, 30, 309, 361]

Specific outcomes for endoscopists performing ≤10 ESDs exceeded the en bloc resection rate of >80%, defined for the early competency, but were below or at the ESGE defined competency thresholds, with global en bloc resection, R0 resection and curative resection rates of 84%, 81% and 75%, respectively.[13, 232] Conversely, endoscopists with >10 procedures surpassed the previous mentioned clinical standards and the outcomes of other Western series.[29, 30, 232, 361] In fact, a trainee is not allowed to practice colonoscopy independently before reaching 200-300 colonoscopies, which is the average number to achieve a 90% cecal intubation rate.[354, 398, 399] Accordingly and taking our results in consideration, ESD expert supervision should be assured, at least in the first 10 human procedures. These findings strongly support the ESGE recommendation in this regard.[232]

We could, hence, assume that a structured training program incorporating simulation on animal models, translates into an effective and safe initial clinical practice. Similar to the benefits of virtual reality simulators for flexible endoscopy, these seem to particularly impact the early learning curve.[26, 337]

Satisfaction with each training program attained a median of 7 (IQR 7-9) out 10 in our study and reached 43% in an Asian survey.[394] In both studies the most valued learning methods were identical, although a greater emphasis was reported on ESD under supervision/ESD observation in the Asian study and on training with animal models in ours.[394] These endoscopists also mentioned that one of the methods needed for better ESD training was to provide Centers for observing/assisting human ESDs performed by experts. Therefore, this goal of observing/assisting and starting ESD under supervision represents the Asian endoscopists preferences and the Western endoscopists´ request. Nevertheless, currently there is a gap between this need and the Western possibility to offer such training, as previously mentioned.

STRENGTHS AND LIMITATIONS

Regarding the strengths of these studies, a wide range of participants from different origins in the world was included, allowing broader perspectives on this topic. It is worth mentioning that in the former study we were able to reach many experts it this field and provide their ESD training, which is frequently overlooked. We would also like to stress that in the later one, besides its innovative concept, data collection was very comprehensive, ranging from the pre training period, containing several steps during training and including ESD clinical implementation with outcomes.

Concerning limitations, we acknowledge the limited number of participants, however fairly acceptable for this type of research, the reliance on self-reported data and the relative modest number of procedures performed. We understand that we reported individual behaviors, which do not inevitably reflect the policy on training of each endoscopic center.

IMPROVING ENDOSCOPIC SUBMUCOSAL DISSECTION TRAINING

GENERAL PRINCIPLES

The growing diversity and complexity of emerging endoscopic techniques poses several challenges to the design and ability to provide specific proper training. [351]

Standardizing principles, goals, contents and teaching approaches ensures uniformization of training. Promoting adequate training of endoscopy trainers is crucial. Particularly, improvement of the ability to consciously deconstruct complex procedures into basic component steps provides an organizational framework for teaching and analyzing trainee performance. Communication and especially the principles of constructive feedback are also essential.

ESD, similarly to other complex endoscopic interventions, is classified as a major skill, in which a new technique or procedure that involves a high level of complexity, interpretative ability, and/or new type of technology is employed. Formal training is strongly advised for the development of such skills.[354]

Criticisms have been made regarding robustness of data substantiating ESD training recommendations previously issued.[351] With this project, a contribution to such an important stage was made. Additionally, the achievements of this thesis can be translated to other techniques, since general principles of proper endoscopy teaching can apply to different endoscopic interventions.

SIMULATION DESIGN

Based on current evidence, endoscopy simulation-based training has been shown to be useful in the early training phase in helping speed up the initial phase of the endoscopy learning curve and reduce patient burden.[22, 23, 26]

Generally, when designing an instructional simulation-based learning, important steps should be followed, such as: (i) determining and establishing the *learning goals* and *objectives*, (ii) selecting a *simulation modality* that best supports the goals and objectives of the simulation (part-task trainers, computer-based, manikin-based, animal-based, simulated/standardized participants, etc.), (iii) choosing a *simulation method* (skills- or scenario-based), (iv) deciding how and when learners will receive *feedback* and *guidance* and (v) considering how learners may be *assessed*.

The *learning goals/objectives* of advanced endoscopic resection techniques have been previously issued and clarified.[232, 240] Regarding *simulation modality*, animal models, particularly live ones present several advantages and are best suited for that purpose, as formerly discussed. They also satisfy the two most common simulation methods, which are skills-based/procedurally focused simulations and scenario-based simulations. In the former, emphasis is set on a specific procedural skill and the objective is skill improvement and mastery.[372, 400] The latter highlights clinical complexity incorporating clinical reasoning, patient management, communication and teamwork. The objective is to work in a ”scenario” as it would occur in clinical practice.[401, 402] Consequently, performing the distinct steps of ESD in a live animal model, which realistically reproduces human procedures, in a setting where both the model and environment resemble the real endoscopy room, fulfills all these requirements.

Therefore, from a global training perspective, it seems the right choice to use simulation with animal models to train ESD.

From the standpoint of its practical implementation, major stages, recognized as fundamental to effective simulation, include preparation, *briefing*, the *simulation activity*, *debriefing/feedback/reflecting* and *evaluation*. Various animal models workshops have been organized worldwide and should rigorously consider these steps. Preparation concerns identifying learners' needs and objectives, as well as designing and assembling all the steps involved in the simulation activity. The *briefing* stage includes faculty and learners. The learning goals are reminded, the logistics, all the simulation phases and respective responsibilities are explained.[403 404] In the *simulation activity,* faculty members should observe, offer specific feedback, assist when necessary, provide time for reflection, ensure equity for all trainees, while assuring that planned goals are accomplished in a safe healthy environment.[405] The *debriefing/feedback/reflecting* phase is fundamental.[406] Feedback may be provided from multiple sources (facilitators, faculty or other experts, peers or simulators themselves) during training or in a post-simulation reflection activity, designated the debriefing. This refers to a guided discussion with the purpose of reflecting and analyzing emotional states, thoughts and actions, providing insight from the experience. The goal is to promote reflective learning to improve clinical performance.[407, 408,409,410, 411] In the *evaluating* section, assessment of efficacy, successes, strengths and limitations of the simulation event may be performed, from the providers and learners´ point of view. Adherence to these principles was ensured in the simulation trainings on animal models that allowed the accomplishment of our studies.

Thus, health care societies could support measures to increase the standards of simulation, investing in development of quality instructional designs to meet all the aforementioned requirements, in order to ensure effective, reliable and reproducible training opportunities.

Integrating simulation in endoscopy training programs should account for the teaching needs, the associated costs and the extent of benefits for patients, trainees, trainers and health care providers. Generally, simulators ought to be validated, easily accessible and affordable for wider implementation.[412] With live animal models many characteristics are met, but price and accessibility will still present a problem in the future.

The proposed 25% or greater reduction in the median number of clinical cases required to achieve the minimal competence, set as a threshold by the American Society for Gastrointestinal Endoscopy (ASGE) Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) initiative, to incorporate a simulator into training, has not been demonstrated, particularly in ESD/EMR animal models.[23, 26, 412]

IN TRAINING ASSESSMENT

Competency assessment of gastrointestinal (GI) endoscopic procedures in training include: procedural volumes, simulation-based assessment, direct observational assessment tools and quality metrics.

Competence thresholds represent minimum numbers of supervised procedures, before competency assessment. We found that endoscopists with >10 human ESDs exceed the ESGE defined competency metrics, supporting the recommendation for expert supervision at least in the first 10 procedures.[232] It is important to acknowledge that the volume of procedures alone does not ensure competence, due to the wide variation in skills acquisition rate between trainees. Therefore, endoscopists with similar experience may present very different levels of proficiency.[351, 413, 414] Furthermore, a learning curve on

ESD is difficult to define due to the different study settings regarding characteristics of lesions included; ESD devices used; presence and degree of supervision; training system followed; trainee experience with animal models; the outcome measured and prior experience with gastric ESD, for non-gastric ESD.[12]

Simulation-based assessment of GI endoscopic skills can be accomplished through motion analysis, performance metrics or direct observational assessment tools, although limited validity evidence is available in this regard.[415-419] Such assessment is surely an attractive tool as it may serve as a proxy for clinical practice, enables reproducible and standardized assessments and allows addressing integrative competencies. However, before its implementation, evidence is required to assure that assessments can reliably distinguish endoscopists with different levels of expertise and that they are predictive of real clinical performance.[420, 421] Trials concerning the assessment of deconstructed tasks in simple simulation boxes appear to correlate with basic and advanced endoscopic procedures, as demonstrated in the Thompson Endoscopic Skills Trainer (TEST; Endo-Sim, LLC) and need further evaluation.[412, 422-424] At the moment, regarding ESD, ESGE proposes quality metrics, such a complete resection rate of at least 80% without perforations during 10 consecutive procedures in animal models before human practice.[232]

The ASGE PIVI initiative proposed that a simulator assessment tool should correlate with minimal competence parameters from real procedures with a kappa value of 0.70 or greater.

Direct observational assessment tools involve external observation and assessment of learners using pre-defined criteria assembled in a framework. These tools represent the best method to identify learning needs, recognize particular deficiencies and enhance useful feedback to trainees. They can have formative or summative purposes and require application over multiple endoscopic procedures to provide reliable information.[425] Taking these assumptions into consideration, these tools are the preferred assessment instruments in training. In order to assure their implementation in ESD training, the items chosen to be assessed should be based on clinically meaningful outcomes. Importantly, reliability and validity evidence of such assessment tools for simulated endoscopy must be a field for future research.[419, 426, 427]

Currently, competence assessment is based on quality metrics, such as en bloc resection rate, R0 resection rate, low risk/curative resection rate and adverse events rate. A minimum number of procedures per/year is also suggested.[13, 232, 251, 360, 363, 364] This approach presents several limitations when applied to training. Performance measures reflect high quality and safe endoscopic care practice, but do not provide continuous evaluation, identification of deficiencies and feedback during the learning process.

Similarly, there is no evidence of their use as surrogate measures of endoscopic skills acquisition during training.[428]

NON-TECHNICAL SKILLS

ESD training programs have emphasized aspects related to cognitive and technical skills. The described non-technical skills focus on communication and teamwork, situation awareness, leadership along with judgement and decision making.[240] These competencies are sometimes undervalued, although they are vital to successful clinical practice, represent recognized core skills related to ESD and are taught and assessed in other endoscopic procedures, such as polypectomies. Efforts should be made to mature skills concerning cooperation in a multidisciplinary team, where knowledge and information are clearly shared for effective patient-centered care; continuous assessment of the situation and problem recognition; support for team members; maintenance of clinical standards; adequate behavior to problem management and options, as well as consideration of possible courses of action.[240, 399] Importantly, these skills should be a target of in training assessments. In this regard, simulators have an untapped potential to improve non-technical aspects of endoscopic performance. Further studies are needed, in particular to evaluate simulation as a mean to train and assess these broader integrative competencies.[330, 428]

PERFORMANCE MEASURES

After adequate training it is fundamental that ESD is undertaken with the highest quality, through compliance with performance measures. Defining such measures should follow a Delphi process and aim at assuring high quality care to patients and protecting society for substandard care.

Its quality measures implementation provides continuous guidance to improvement in performance, allowing adequate educational interventions.

One concern that should be taken into consideration before setting quality indicators is the probability of its real dissemination and implementation. Some already verified barriers preventing the adoption of performance measures for many procedures in routine practice, including lack of motivation, resources, and/or leadership, should be a matter of reflection. [429-435]

These indicators ought to be susceptible for improvement, have proven impact on significant clinical outcomes or quality of life and must be well-defined, reliable and simple to assess. They should not increase the administrative load or be time consuming. Indicators shall be prioritized according to each country, applicable to all levels of endoscopic services, implemented or endorsed by endoscopic societies and aided by information technology systems, ideally using full electronic reporting with standardized protocols with integrated automated capture and feedback of performance measures.[429-433, 435]

CONCLUSION

A structured curriculum for ESD, should be based on competencies that a trainee should present at the end of the program. These must be adequately defined, specific, measurable entities, such as units of knowledge, skill, behavior, expertise, that translate into clinical competence. Care must be taken to ensure adequacy to a challenging professional practice in order to enable collecting and processing of information, producing accurate assessments and decisions, solving problems, making interventions, as well as interacting with peers, colleagues and patients. The ultimate goal is to provide the best possible health care. To achieve this, it is essential to integrate personal, interpersonal, ethical, financial, managerial, multiprofessional and evidence-based dimensions of Medicine.[436, 437]

IX. Conclusions and future perspectives

CONCLUSIONS

The role and dissemination of advanced endoscopic resection techniques are expected to grow in the upcoming years. Considering its complexity, training programs have been suggested to provide its effective and safe clinical implementation.

The training principles explored in this thesis can be applied in several other challenging techniques, through particular adjustments.

Using ESD as an example, we investigated the complete training trajectory on a complex and demanding procedure. It was possible to start from the choice of the adequate simulator, its basic validation and to go through the evaluation of the learning curve for that technique, on that specific model. The existing training methods used in referral centers were assessed and ultimately, translation to clinical practice of structured teaching programs was evaluated.

Practicing EMR and ESD on live animal models was considered very realistic compared to the human setting and highly appreciated as a learning tool. Validation of the model for such training was established and an improvement in ESD performance measures was documented, reflected by an increase in complete resection rate, en bloc resection rate, ESD speed and a decrease in the adverse event rate. It was considered very useful and a prerequisite before clinical practice.

Therefore, adequate evidence is available substantiating the role of this model in the pre-clinical learning phase and regarding the relevance of its incorporation into formal training programs.

Western endoscopists had extensive endoscopic experience before starting ESD and the majority had pre-clinical training with animal models. Similarly, participants of ESD workshops were adequately skilled prior to clinical ESD, complying with most of recommendations for training and appropriately implementing the technique in clinical practice. Transfer to human practice of prior ESD skills obtained in these hands-on training courses was recognized. Finally, we concluded that structured training programs were able to provide achievement of clinical outcomes exceeding established standards, namely in the early clinical phase.

Our findings support the implementation of structured training programs for complex endoscopic procedures, which will provide guidance for health care societies, offer the proper resources for endoscopists and impact patients, through effectiveness and safety in clinical practice.

FUTURE PERSPECTIVES

The field of gastrointestinal therapeutic endoscopy is progressing at high pace.

Complexity grading scales based on the difficulty of the procedure could be explored, with the goal of its incorporation in ESD curricula, similarly to what has occurred in Endoscopic Retrograde Cholangiopancreatography (ERCP).[438-441] These might predict success and adverse event rate in clinical practice.[442] Lesion´s location, access, size and other characteristics could be taken into consideration.

Since training programs have focused mainly on ESD cognitive and technical skills, studies should address the best approach to the integration of non-technical skills, as well as its assessment.

Standardization of the design of simulation-based learning in such techniques and formal education of tutors in its different stages should be accomplished. A larger body of evidence on direct clinical benefits of prior animal training, namely regarding transfer of skills to patient-based procedures, should be pursued. Given the demonstrated benefits of such training, prospective comparative studies on ESD practice, with and without prior animal model exposure, seem inappropriate by the absence of common sense and ethical responsibility, exposing patients to potential preventable risks. Nevertheless, data on the training capacity between different live animal models and on the potential different role of ex vivo and live animal models should be pursued. Additionally, defining success and competency thresholds for ESD simulation with animal models should be sought and should take into account the type of animal and its ex or in vivo nature.

Fields like feedback and assessment integration into training require further research. Debriefing facilitator rating tools could be developed, specifically for ESD. Similarly, the role of assessment of performance or competence during training, through simulation or patient-based endoscopy should be evaluated. Deconstructed tasks to perform ESD might be explored and direct observation assessment tools, as described for upper endoscopy, lower endoscopy, polypectomy, ERCP and EUS could be investigated. Formative assessments that address the process and summative assessments that would lead to certification, establishing competence for autonomous practice, focusing on the result, should be developed. Such assessments should follow a thorough validation process.

Minimal clinical thresholds procedures before assessment of competency could be defined more rigorously, despite its inherent limitations and ideally considering each organ individually. For this purpose, constraints regarding distinct previous endoscopic experience, training pathways, namely simulation exposure and types of lesions, must be considered to allow uniformization.

X. REFERENCES

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-42410.3322/caac.21492
2. Liu Q, Ding L, Qiu X, Meng F. Updated evaluation of endoscopic submucosal dissection versus surgery for early gastric cancer: A systematic review and meta-analysis. Int J Surg. 2020;73:28-4110.1016/j.ijsu.2019.11.027
3. Libânio D, Braga V, Ferraz S, Castro R, Lage J, Pita I, et al. Prospective comparative study of endoscopic submucosal dissection and gastrectomy for early neoplastic lesions including patients' perspectives. Endoscopy. 2019;51(1):30-910.1055/a-0628-6601
4. Cao Y, Liao C, Tan A, Gao Y, Mo Z, Gao F. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. Endoscopy. 2009;41(9):751-710.1055/s-0029-1215053
5. 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(9):829-5410.1055/s-0034-1392882
6. Siau K, Hawkes ND, Dunckley P. Training in Endoscopy. Curr Treat Options Gastroenterol. 2018;16(3):345-6110.1007/s11938-018-0191-1
7. Oda I, Odagaki T, Suzuki H, Nonaka S, Yoshinaga S. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc. 2012;24 Suppl 1:129-3210.1111/j.1443-1661.2012.01265.x
8. Yamamoto Y, Fujisaki J, Ishiyama A, Hirasawa T, Igarashi M. Current status of training for endoscopic submucosal dissection for gastric epithelial neoplasm at Cancer Institute Hospital, Japanese Foundation for Cancer Research, a famous Japanese hospital. Dig Endosc. 2012;24 Suppl 1:148-5310.1111/j.1443-1661.2012.01278.x
9. Terasaki M, Tanaka S, Oka S, Nakadoi K, Takata S, Kanao H, et al. Clinical outcomes of endoscopic submucosal dissection and endoscopic mucosal resection for laterally spreading tumors larger than 20 mm. Journal of gastroenterology and hepatology. 2012;27(4):734-4010.1111/j.1440-1746.2011.06977.x
10. Toyokawa T, Inaba T, Omote S, Okamoto A, Miyasaka R, Watanabe K, et al. Risk factors for perforation and delayed bleeding associated with endoscopic submucosal dissection for early gastric neoplasms: analysis of 1123 lesions. Journal of gastroenterology and hepatology. 2012;27(5):907-1210.1111/j.1440-1746.2011.07039.x
11. Probst A, Golger D, Anthuber M, Markl B, Messmann H. Endoscopic submucosal dissection in large sessile lesions of the rectosigmoid: learning curve in a European center. Endoscopy. 2012;44(7):660-710.1055/s-0032-1309403
12. Coman RM, Gotoda T, Draganov PV. Training in endoscopic submucosal dissection. World J Gastrointest Endosc. 2013;5(8):369-78.PMC3742702 10.4253/wjge.v5.i8.369
13. Oyama T, Yahagi N, Ponchon T, Kiesslich T, Berr F. How to establish endoscopic submucosal dissection in Western countries. World J Gastroenterol. 2015;21(40):11209-20.PMC4616199 10.3748/wjg.v21.i40.11209
14. 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(10):853-810.1055/s-0030-1255563
15. 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. Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society. 2011;23(4):281-910.1111/j.1443-1661.2011.01129.x
16. Parra-Blanco A, Arnau MR, Nicolas-Perez D, Gimeno-Garcia AZ, Gonzalez N, Diaz-Acosta JA, et al. Endoscopic submucosal dissection training with pig models in a Western country. World journal of gastroenterology. 2010;16(23):2895-900.2887585
17. Vazquez-Sequeiros E, de Miquel DB, Olcina JR, Martin JA, Garcia M, Lucas DJ, et al. Training model for teaching endoscopic submucosal dissection of gastric tumors. Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva. 2009;101(8):546-52
18. Gerson LB, Van Dam J. Technology review: the use of simulators for training in GI endoscopy. Gastrointestinal endoscopy. 2004;60(6):992-1001
19. Herreros de Tejada A. ESD training: A challenging path to excellence. World J Gastrointest Endosc. 2014;6(4):112-20.PMC3985151 10.4253/wjge.v6.i4.112
20. Bok GH, Cho JY. ESD Hands-on Course Using Ex Vivo and In Vivo Models in South Korea. Clinical endoscopy. 2012;45(4):358-61.3521936 10.5946/ce.2012.45.4.358
21. 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(11):933-4010.1055/s-0034-1377348

22. Singh S, Sedlack RE, Cook DA. Effects of simulation-based training in gastrointestinal endoscopy: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2014;12(10):1611-23.e410.1016/j.cgh.2014.01.037
23. Khan R, Plahouras J, Johnston BC, Scaffidi MA, Grover SC, Walsh CM. Virtual reality simulation training for health professions trainees in gastrointestinal endoscopy. Cochrane Database Syst Rev. 2018;8(8):Cd008237.PMC6513657 10.1002/14651858.CD008237.pub3
24. Meng W, Yue P, Leung JW, Wang H, Wang X, Wang F, et al. Impact of mechanical simulator practice on clinical ERCP performance by novice surgical trainees: a randomized controlled trial. Endoscopy. 2020;52(11):1004-1310.1055/a-1217-6727
25. Catharine M. Walsh JC. Clinical Gastrointestinal Endoscopy: Elsevier, Inc; 2019.
26. Ekkelenkamp VE, Koch AD, de Man RA, Kuipers EJ. Training and competence assessment in GI endoscopy: a systematic review. Gut. 2016;65(4):607-1510.1136/gutjnl-2014-307173
27. Martinek J, Suchanek S, Stefanova M, Rotnaglova B, Zavada F, Strosova A, et al. Training on an ex vivo animal model improves endoscopic skills: a randomized, single-blind study. Gastrointest Endosc. 2011;74(2):367-7310.1016/j.gie.2011.04.042
28. Maiss J, Prat F, Wiesnet J, Proeschel A, Matthes K, Peters A, et al. The complementary Erlangen active simulator for interventional endoscopy training is superior to solely clinical education in endoscopic hemostasis--the French training project: a prospective trial. Eur J Gastroenterol Hepatol. 2006;18(11):1217-2510.1097/01.meg.0000236881.28967.41
29. Maselli R, Iacopini F, Azzolini F, Petruzziello L, Manno M, De Luca L, et al. Endoscopic submucosal dissection: Italian national survey on current practices, training and outcomes. Dig Liver Dis. 2020;52(1):64-7110.1016/j.dld.2019.09.009
30. 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(1):45-53.PMC5384549 10.1177/2050640616644392
31. Ferlay J LM, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F Global Cancer Observatory: Cancer Tomorrow Lyon, France: International Agency for Research on Cancer2020 [Available from: https://gco.iarc.fr/tomorrow.
32. Survival of Cancer Patients in Europe. Eurocare 5 database 2021 [Available from: https://w3.iss.it/site/EU5Results/.
33. Fitzmaurice C, Dicker D, Pain A, Hamavid H, Moradi-Lakeh M, MacIntyre MF, et al. The Global Burden of Cancer 2013. JAMA Oncol. 2015;1(4):505-27.PMC4500822 10.1001/jamaoncol.2015.0735
34. Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 2017;3(4):524-48.PMC6103527 10.1001/jamaoncol.2016.5688
35. Edgren G, Adami HO, Weiderpass E, Nyrén O. A global assessment of the oesophageal adenocarcinoma epidemic. Gut. 2013;62(10):1406-1410.1136/gutjnl-2012-302412
36. Brown LM, Devesa SS, Chow WH. Incidence of adenocarcinoma of the esophagus among white Americans by sex, stage, and age. J Natl Cancer Inst. 2008;100(16):1184-7.PMC2518165 10.1093/jnci/djn211
37. Blot WJ, McLaughlin JK. The changing epidemiology of esophageal cancer. Semin Oncol. 1999;26(5 Suppl 15):2-8
38. Lagergren J, Smyth E, Cunningham D, Lagergren P. Oesophageal cancer. Lancet. 2017;390(10110):2383-9610.1016/s0140-6736(17)31462-9
39. Kauppila JH, Mattsson F, Brusselaers N, Lagergren J. Prognosis of oesophageal adenocarcinoma and squamous cell carcinoma following surgery and no surgery in a nationwide Swedish cohort study. BMJ Open. 2018;8(5):e021495.PMC5950652 10.1136/bmjopen-2018-021495
40. Bollschweiler E, Schröder W, Hölscher AH, Siewert JR. Preoperative risk analysis in patients with adenocarcinoma or squamous cell carcinoma of the oesophagus. Br J Surg. 2000;87(8):1106-1010.1046/j.1365-2168.2000.01474.x
41. Wang QL, Ness-Jensen E, Santoni G, Xie SH, Lagergren J. Development and Validation of a Risk Prediction Model for Esophageal Squamous Cell Carcinoma Using Cohort Studies. Am J Gastroenterol. 2021;116(4):683-9110.14309/ajg.0000000000001094
42. Wiseman M. The second World Cancer Research Fund/American Institute for Cancer Research expert report. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Proc Nutr Soc. 2008;67(3):253-610.1017/s002966510800712x
43. Jain KS, Sikora AG, Baxi SS, Morris LG. Synchronous cancers in patients with head and neck cancer: risks in the era of human papillomavirus-associated oropharyngeal cancer. Cancer. 2013;119(10):1832-710.1002/cncr.27988
44. Wang YK, Chuang YS, Wu TS, Lee KW, Wu CW, Wang HC, et al. Endoscopic screening for synchronous esophageal neoplasia among patients with incident head and neck cancer: Prevalence, risk factors, and outcomes. Int J Cancer. 2017;141(10):1987-9610.1002/ijc.30911
45. Scherübl H, von Lampe B, Faiss S, Däubler P, Bohlmann P, Plath T, et al. Screening for oesophageal neoplasia in patients with head and neck cancer. Br J Cancer. 2002;86(2):239-43.PMC2375180 10.1038/sj.bjc.6600018

46. Su YY, Chen WC, Chuang HC, Guo CS, Lin YT, Luo SD, et al. Effect of routine esophageal screening in patients with head and neck cancer. JAMA Otolaryngol Head Neck Surg. 2013;139(4):350-410.1001/jamaoto.2013.46
47. Katada C, Yokoyama T, Yano T, Kaneko K, Oda I, Shimizu Y, et al. Alcohol Consumption and Multiple Dysplastic Lesions Increase Risk of Squamous Cell Carcinoma in the Esophagus, Head, and Neck. Gastroenterology. 2016;151(5):860-9.e710.1053/j.gastro.2016.07.040
48. Urabe Y, Hiyama T, Tanaka S, Oka S, Yoshihara M, Arihiro K, et al. Metachronous multiple esophageal squamous cell carcinomas and Lugol-voiding lesions after endoscopic mucosal resection. Endoscopy. 2009;41(4):304-910.1055/s-0029-1214477
49. Fukuhara T, Hiyama T, Tanaka S, Oka S, Yoshihara M, Arihiro K, et al. Characteristics of esophageal squamous cell carcinomas and lugol-voiding lesions in patients with head and neck squamous cell carcinoma. J Clin Gastroenterol. 2010;44(2):e27-3310.1097/MCG.0b013e3181b31325
50. Zagari RM, Marasco G, Tassi V, Ferretti S, Lugaresi M, Fortunato F, et al. Risk of Squamous Cell Carcinoma and Adenocarcinoma of the Esophagus in Patients With Achalasia: A Long-Term Prospective Cohort Study in Italy. Am J Gastroenterol. 2021;116(2):289-9510.14309/ajg.0000000000000955
51. Leeuwenburgh I, Scholten P, Alderliesten J, Tilanus HW, Looman CW, Steijerberg EW, et al. Long-term esophageal cancer risk in patients with primary achalasia: a prospective study. Am J Gastroenterol. 2010;105(10):2144-910.1038/ajg.2010.263
52. Zendehdel K, Nyrén O, Edberg A, Ye W. Risk of esophageal adenocarcinoma in achalasia patients, a retrospective cohort study in Sweden. Am J Gastroenterol. 2011;106(1):57-6110.1038/ajg.2010.449
53. Streitz JM, Jr., Ellis FH, Jr., Gibb SP, Heatley GM. Achalasia and squamous cell carcinoma of the esophagus: analysis of 241 patients. Ann Thorac Surg. 1995;59(6):1604-910.1016/0003-4975(94)00997-l
54. Tustumi F, Bernardo WM, da Rocha JRM, Szachnowicz S, Seguro FC, Bianchi ET, et al. Esophageal achalasia: a risk factor for carcinoma. A systematic review and meta-analysis. Dis Esophagus. 2017;30(10):1-810.1093/dote/dox072
55. Ellis A, Risk JM, Maruthappu T, Kelsell DP. Tylosis with oesophageal cancer: Diagnosis, management and molecular mechanisms. Orphanet J Rare Dis. 2015;10:126.PMC4589029 10.1186/s13023-015-0346-2
56. Varela AB, Blanco Rodríguez MM, Boullosa PE, Silva JG. Tylosis A with squamous cell carcinoma of the oesophagus in a Spanish family. Eur J Gastroenterol Hepatol. 2011;23(3):286-810.1097/MEG.0b013e328344042d
57. Risk JM, Mills HS, Garde J, Dunn JR, Evans KE, Hollstein M, et al. The tylosis esophageal cancer (TOC) locus: more than just a familial cancer gene. Dis Esophagus. 1999;12(3):173-610.1046/j.1442-2050.1999.00042.x
58. Castellsagué X, Muñoz N, De Stefani E, Victora CG, Castelletto R, Rolón PA. Influence of mate drinking, hot beverages and diet on esophageal cancer risk in South America. Int J Cancer. 2000;88(4):658-6410.1002/1097-0215(20001115)88:4<658::aid-ijc22>3.0.co;2-t
59. Islami F, Boffetta P, Ren JS, Pedoeim L, Khatib D, Kamangar F. High-temperature beverages and foods and esophageal cancer risk--a systematic review. Int J Cancer. 2009;125(3):491-524.PMC2773211 10.1002/ijc.24445
60. Chen Y, Tong Y, Yang C, Gan Y, Sun H, Bi H, et al. Consumption of hot beverages and foods and the risk of esophageal cancer: a meta-analysis of observational studies. BMC Cancer. 2015;15:449.PMC4457273 10.1186/s12885-015-1185-1
61. Millar AJ, Cox SG. Caustic injury of the oesophagus. Pediatr Surg Int. 2015;31(2):111-2110.1007/s00383-014-3642-3
62. Isolauri J, Markkula H. Lye ingestion and carcinoma of the esophagus. Acta Chir Scand. 1989;155(4-5):269-71
63. Thrift AP. The epidemic of oesophageal carcinoma: Where are we now? Cancer Epidemiol. 2016;41:88-9510.1016/j.canep.2016.01.013
64. Shaheen NJ, Falk GW, Iyer PG, Gerson LB. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. Am J Gastroenterol. 2016;111(1):30-50; quiz 110.1038/ajg.2015.322
65. Dong J, Buas MF, Gharahkhani P, Kendall BJ, Onstad L, Zhao S, et al. Determining Risk of Barrett's Esophagus and Esophageal Adenocarcinoma Based on Epidemiologic Factors and Genetic Variants. Gastroenterology. 2018;154(5):1273-81.e3.PMC5880715 10.1053/j.gastro.2017.12.003
66. Rubenstein JH, Scheiman JM, Sadeghi S, Whiteman D, Inadomi JM. Esophageal adenocarcinoma incidence in individuals with gastroesophageal reflux: synthesis and estimates from population studies. Am J Gastroenterol. 2011;106(2):254-60.PMC3901355 10.1038/ajg.2010.470
67. Spechler SJ, Goyal RK. The columnar-lined esophagus, intestinal metaplasia, and Norman Barrett. Gastroenterology. 1996;110(2):614-2110.1053/gast.1996.v110.agast960614
68. Fitzgerald RC, di Pietro M, Ragunath K, Ang Y, Kang JY, Watson P, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Gut. 2014;63(1):7-4210.1136/gutjnl-2013-305372
69. de Jonge PJ, van Blankenstein M, Grady WM, Kuipers EJ. Barrett's oesophagus: epidemiology, cancer risk and implications for management. Gut. 2014;63(1):191-202.PMC6597262 10.1136/gutjnl-2013-305490
70. Bennett C, Moayyedi P, Corley DA, DeCaestecker J, Falck-Ytter Y, Falk G, et al. BOB CAT: A Large-Scale Review and Delphi Consensus for Management of Barrett's Esophagus With No Dysplasia, Indefinite for, or Low-Grade Dysplasia. Am J Gastroenterol. 2015;110(5):662-82; quiz 83.PMC4436697 10.1038/ajg.2015.55

71. Thrift AP. Global burden and epidemiology of Barrett oesophagus and oesophageal cancer. Nat Rev Gastroenterol Hepatol. 2021;18(6):432-4310.1038/s41575-021-00419-3
72. Rubenstein JH, McConnell D, Waljee AK, Metko V, Nofz K, Khodadost M, et al. Validation and Comparison of Tools for Selecting Individuals to Screen for Barrett's Esophagus and Early Neoplasia. Gastroenterology. 2020;158(8):2082-92.PMC7282990 10.1053/j.gastro.2020.02.037
73. di Pietro M, Chan D, Fitzgerald RC, Wang KK. Screening for Barrett's Esophagus. Gastroenterology. 2015;148(5):912-23.PMC4703087 10.1053/j.gastro.2015.02.012
74. Camargo MC, Anderson WF, King JB, Correa P, Thomas CC, Rosenberg PS, et al. Divergent trends for gastric cancer incidence by anatomical subsite in US adults. Gut. 2011;60(12):1644-9.PMC3202077 10.1136/gut.2010.236737
75. Anderson WF, Camargo MC, Fraumeni JF, Jr., Correa P, Rosenberg PS, Rabkin CS. Age-specific trends in incidence of noncardia gastric cancer in US adults. Jama. 2010;303(17):1723-8.PMC3142962 10.1001/jama.2010.496
76. Thrift AP, Nguyen TH. Gastric Cancer Epidemiology. Gastrointest Endosc Clin N Am. 2021;31(3):425-3910.1016/j.giec.2021.03.001
77. Anderson WF, Rabkin CS, Turner N, Fraumeni JF, Jr., Rosenberg PS, Camargo MC. The Changing Face of Noncardia Gastric Cancer Incidence Among US Non-Hispanic Whites. J Natl Cancer Inst. 2018;110(6):608-15.PMC6005150 10.1093/jnci/djx262
78. Thrift AP, El-Serag HB. Burden of Gastric Cancer. Clin Gastroenterol Hepatol. 2020;18(3):534-4210.1016/j.cgh.2019.07.045
79. Abe H, Ushiku T. Pathological Diversity of Gastric Cancer from the Viewpoint of Background Condition. Digestion. 2021:1-910.1159/000519337
80. Libânio D, Rodrigues JR, Bento MJ, Ebigbo A, Messmann H, Verhoeven R, et al. Gastric cancer incidence and mortality trends between 2007-2016 in three European countries. Endoscopy. 202110.1055/a-1673-1118
81. Mattiuzzi C, Lippi G. Current Cancer Epidemiology. J Epidemiol Glob Health. 2019;9(4):217-22.PMC7310786 10.2991/jegh.k.191008.001
82. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. Cancer Epidemiol Biomarkers Prev. 2014;23(5):700-13.PMC4019373 10.1158/1055-9965.Epi-13-1057
83. Huang RJ, Epplein M, Hamashima C, Choi IJ, Lee E, Deapen D, et al. An Approach to the Primary and Secondary Prevention of Gastric Cancer in the United States. Clin Gastroenterol Hepatol. 202110.1016/j.cgh.2021.09.039
84. Plummer M, Franceschi S, Vignat J, Forman D, de Martel C. Global burden of gastric cancer attributable to Helicobacter pylori. Int J Cancer. 2015;136(2):487-9010.1002/ijc.28999
85. Saumoy M, Schneider Y, Shen N, Kahaleh M, Sharaiha RZ, Shah SC. Cost Effectiveness of Gastric Cancer Screening According to Race and Ethnicity. Gastroenterology. 2018;155(3):648-6010.1053/j.gastro.2018.05.026
86. Ocasio Quinones GA, Woolf A. Small Bowel Cancer. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.; 2021.
87. Qubaiah O, Devesa SS, Platz CE, Huycke MM, Dores GM. Small intestinal cancer: a population-based study of incidence and survival patterns in the United States, 1992 to 2006. Cancer Epidemiol Biomarkers Prev. 2010;19(8):1908-18.PMC2919612 10.1158/1055-9965.Epi-10-0328
88. Maguire A, Sheahan K. Primary small bowel adenomas and adenocarcinomas-recent advances. Virchows Arch. 2018;473(3):265-7310.1007/s00428-018-2400-7
89. Ferlay J, Colombet M, Soerjomataram I, Dyba T, Randi G, Bettio M, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer. 2018;103:356-8710.1016/j.ejca.2018.07.005
90. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. Nat Rev Gastroenterol Hepatol. 2019;16(12):713-3210.1038/s41575-019-0189-8
91. Imamura F, Micha R, Khatibzadeh S, Fahimi S, Shi P, Powles J, et al. Dietary quality among men and women in 187 countries in 1990 and 2010: a systematic assessment. Lancet Glob Health. 2015;3(3):e132-42.PMC4342410 10.1016/s2214-109x(14)70381-x
92. Schreuders EH, Ruco A, Rabeneck L, Schoen RE, Sung JJ, Young GP, et al. Colorectal cancer screening: a global overview of existing programmes. Gut. 2015;64(10):1637-4910.1136/gutjnl-2014-309086
93. Dekker E, Rex DK. Advances in CRC Prevention: Screening and Surveillance. Gastroenterology. 2018;154(7):1970-8410.1053/j.gastro.2018.01.069
94. Crockett SD, Nagtegaal ID. Terminology, Molecular Features, Epidemiology, and Management of Serrated Colorectal Neoplasia. Gastroenterology. 2019;157(4):949-66.e410.1053/j.gastro.2019.06.041
95. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. Lancet. 2019;394(10207):1467-8010.1016/s0140-6736(19)32319-0
96. Laiyemo AO, Doubeni C, Pinsky PF, Doria-Rose VP, Bresalier R, Lamerato LE, et al. Race and colorectal cancer disparities: health-care utilization vs different cancer susceptibilities. J Natl Cancer Inst. 2010;102(8):538-46.PMC2857802 10.1093/jnci/djq068
97. Laiyemo AO, Doubeni C, Pinsky PF, Doria-Rose VP, Bresalier R, Hickey T, et al. Occurrence of Distal Colorectal Neoplasia Among Whites and Blacks Following Negative Flexible Sigmoidoscopy: An Analysis of PLCO Trial. J Gen Intern Med. 2015;30(10):1447-53.PMC4579215 10.1007/s11606-015-3297-3

98. Imperiale TF, Abhyankar PR, Stump TE, Emmett TW. Prevalence of Advanced, Precancerous Colorectal Neoplasms in Black and White Populations: A Systematic Review and Meta-analysis. Gastroenterology. 2018;155(6):1776-86.e110.1053/j.gastro.2018.08.020
99. Rutter CM, Knudsen AB, Lin JS, Bouskill KE. Black and White Differences in Colorectal Cancer Screening and Screening Outcomes: A Narrative Review. Cancer Epidemiol Biomarkers Prev. 2021;30(1):3-12.PMC7855228 10.1158/1055-9965.Epi-19-1537
100. Siegel RL, Jemal A. Percentage of colorectal cancer diagnosed in adults aged younger than 50 years. Cancer. 2016;122(9):1462-310.1002/cncr.29980
101. Peterse EFP, Meester RGS, Siegel RL, Chen JC, Dwyer A, Ahnen DJ, et al. The impact of the rising colorectal cancer incidence in young adults on the optimal age to start screening: Microsimulation analysis I to inform the American Cancer Society colorectal cancer screening guideline. Cancer. 2018;124(14):2964-73.PMC6033623 10.1002/cncr.31543
102. Imperiale TF, Kahi CJ, Rex DK. Lowering the Starting Age for Colorectal Cancer Screening to 45 Years: Who Will Come…and Should They? Clin Gastroenterol Hepatol. 2018;16(10):1541-410.1016/j.cgh.2018.08.023
103. Henrikson NB, Webber EM, Goddard KA, Scrol A, Piper M, Williams MS, et al. Family history and the natural history of colorectal cancer: systematic review. Genet Med. 2015;17(9):702-12.PMC4955831 10.1038/gim.2014.188
104. Schoen RE, Razzak A, Yu KJ, Berndt SI, Firl K, Riley TL, et al. Incidence and mortality of colorectal cancer in individuals with a family history of colorectal cancer. Gastroenterology. 2015;149(6):1438-45.e1.PMC4628587 10.1053/j.gastro.2015.07.055
105. Johns LE, Houlston RS. A systematic review and meta-analysis of familial colorectal cancer risk. Am J Gastroenterol. 2001;96(10):2992-300310.1111/j.1572-0241.2001.04677.x
106. Samadder NJ, Curtin K, Tuohy TM, Rowe KG, Mineau GP, Smith KR, et al. Increased risk of colorectal neoplasia among family members of patients with colorectal cancer: a population-based study in Utah. Gastroenterology. 2014;147(4):814-21.e5; quiz e15-610.1053/j.gastro.2014.07.006
107. Jacobs ET, Gupta S, Baron JA, Cross AJ, Lieberman DA, Murphy G, et al. Family history of colorectal cancer in first-degree relatives and metachronous colorectal adenoma. Am J Gastroenterol. 2018;113(6):899-905.PMC8283793 10.1038/s41395-018-0007-x
108. Syngal S, Brand RE, Church JM, Giardiello FM, Hampel HL, Burt RW. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. Am J Gastroenterol. 2015;110(2):223-62; quiz 63.PMC4695986 10.1038/ajg.2014.435
109. Mork ME, You YN, Ying J, Bannon SA, Lynch PM, Rodriguez-Bigas MA, et al. High Prevalence of Hereditary Cancer Syndromes in Adolescents and Young Adults With Colorectal Cancer. J Clin Oncol. 2015;33(31):3544-9.PMC4979241 potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article. 10.1200/jco.2015.61.4503
110. Jasperson KW, Tuohy TM, Neklason DW, Burt RW. Hereditary and familial colon cancer. Gastroenterology. 2010;138(6):2044-58.PMC3057468 10.1053/j.gastro.2010.01.054
111. Samadder NJ, Jasperson K, Burt RW. Hereditary and common familial colorectal cancer: evidence for colorectal screening. Dig Dis Sci. 2015;60(3):734-4710.1007/s10620-014-3465-z
112. Laukoetter MG, Mennigen R, Hannig CM, Osada N, Rijcken E, Vowinkel T, et al. Intestinal cancer risk in Crohn's disease: a meta-analysis. J Gastrointest Surg. 2011;15(4):576-8310.1007/s11605-010-1402-9
113. Lee YN, Lee JL, Yu CS, Kim JB, Lim SB, Park IJ, et al. Clinicopathological Characteristics and Surgical Outcomes of Crohn Disease-Associated Colorectal Malignancy. Ann Coloproctol. 2021;37(2):101-8.PMC8134931 10.3393/ac.2020.11.02
114. Wijnands AM, Mahmoud R, Lutgens M, Oldenburg B. Surveillance and management of colorectal dysplasia and cancer in inflammatory bowel disease: Current practice and future perspectives. Eur J Intern Med. 202110.1016/j.ejim.2021.08.010
115. Brenner H, Chang-Claude J, Seiler CM, Rickert A, Hoffmeister M. Protection from colorectal cancer after colonoscopy: a population-based, case-control study. Ann Intern Med. 2011;154(1):22-3010.7326/0003-4819-154-1-201101040-00004
116. Fournel I, Cottet V, Binquet C, Jooste V, Faivre J, Bouvier AM, et al. Rural-urban differences in the long-term risk of colorectal cancer after adenoma removal: a population-based study. Dig Liver Dis. 2014;46(4):376-8210.1016/j.dld.2013.12.018
117. Cottet V, Jooste V, Fournel I, Bouvier AM, Faivre J, Bonithon-Kopp C. Long-term risk of colorectal cancer after adenoma removal: a population-based cohort study. Gut. 2012;61(8):1180-610.1136/gutjnl-2011-300295
118. Imperiale TF, Juluri R, Sherer EA, Glowinski EA, Johnson CS, Morelli MS. A risk index for advanced neoplasia on the second surveillance colonoscopy in patients with previous adenomatous polyps. Gastrointest Endosc. 2014;80(3):471-810.1016/j.gie.2014.03.042
119. Honda M, Naoe H, Gushima R, Miyamoto H, Tateyama M, Sakurai K, et al. Risk stratification for advanced colorectal neoplasia based on the findings of the index and first surveillance colonoscopies. PLoS One. 2021;16(1):e0245211.PMC7822265 10.1371/journal.pone.0245211
120. Xu X, Yu E, Gao X, Song N, Liu L, Wei X, et al. Red and processed meat intake and risk of colorectal adenomas: a meta-analysis of observational studies. Int J Cancer. 2013;132(2):437-4810.1002/ijc.27625
121. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. Bmj. 2017;356:j477.PMC5421437

www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. 10.1136/bmj.j477
122. Botteri E, Borroni E, Sloan EK, Bagnardi V, Bosetti C, Peveri G, et al. Smoking and Colorectal Cancer Risk, Overall and by Molecular Subtypes: A Meta-Analysis. Am J Gastroenterol. 2020;115(12):1940-910.14309/ajg.0000000000000803
123. Cai S, Li Y, Ding Y, Chen K, Jin M. Alcohol drinking and the risk of colorectal cancer death: a meta-analysis. Eur J Cancer Prev. 2014;23(6):532-910.1097/cej.0000000000000076
124. Nakatsu G, Li X, Zhou H, Sheng J, Wong SH, Wu WK, et al. Gut mucosal microbiome across stages of colorectal carcinogenesis. Nat Commun. 2015;6:8727.PMC4640069 10.1038/ncomms9727
125. Zhang Y, Yu X, Yu E, Wang N, Cai Q, Shuai Q, et al. Changes in gut microbiota and plasma inflammatory factors across the stages of colorectal tumorigenesis: a case-control study. BMC Microbiol. 2018;18(1):92.PMC6114884 10.1186/s12866-018-1232-6
126. Kwong TNY, Wang X, Nakatsu G, Chow TC, Tipoe T, Dai RZW, et al. Association Between Bacteremia From Specific Microbes and Subsequent Diagnosis of Colorectal Cancer. Gastroenterology. 2018;155(2):383-90.e810.1053/j.gastro.2018.04.028
127. Săftoiu A, Hassan C, Areia M, Bhutani MS, Bisschops R, Bories E, et al. Role of gastrointestinal endoscopy in the screening of digestive tract cancers in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2020;52(4):293-30410.1055/a-1104-5245
128. Robra BP. Harms and Benefits of Cancer Screening. Recent Results Cancer Res. 2021;218:85-10410.1007/978-3-030-63749-1_7
129. Jacklyn G, Bell K, Hayen A. Assessing the efficacy of cancer screening. Public Health Res Pract. 2017;27(3)10.17061/phrp2731727
130. Carter JL, Coletti RJ, Harris RP. Quantifying and monitoring overdiagnosis in cancer screening: a systematic review of methods. Bmj. 2015;350:g7773.PMC4332263 10.1136/bmj.g7773
131. Caverly TJ, Hayward RA, Reamer E, Zikmund-Fisher BJ, Connochie D, Heisler M, et al. Presentation of Benefits and Harms in US Cancer Screening and Prevention Guidelines: Systematic Review. J Natl Cancer Inst. 2016;108(6):djv436.PMC5009951 10.1093/jnci/djv436
132. van Heijningen EM, Lansdorp-Vogelaar I, Steyerberg EW, Goede SL, Dekker E, Lesterhuis W, et al. Adherence to surveillance guidelines after removal of colorectal adenomas: a large, community-based study. Gut. 2015;64(10):1584-92.PMC4602240 10.1136/gutjnl-2013-306453
133. Koh FH, Chan DKH, Ng J, Tan KK. Adherence to surveillance guidelines following colonic polypectomy is abysmal. J Gastrointest Oncol. 2019;10(2):166-70.PMC6465487 10.21037/jgo.2018.11.06
134. Oh CK, Aniwan S, Piyachaturawat P, Wong Z, Soe T, Luvsandagva B, et al. Adherence to Surveillance Guidelines after the Removal of Colorectal Polyps: A Multinational, Multicenter, Prospective Survey. Gut Liver. 202110.5009/gnl20166
135. Crockett SD, Lipkus IM, Bright SD, Sampliner RE, Wang KK, Boolchand V, et al. Overutilization of endoscopic surveillance in nondysplastic Barrett's esophagus: a multicenter study. Gastrointest Endosc. 2012;75(1):23-31.e2.PMC3961007 10.1016/j.gie.2011.08.042
136. Tavakkoli A, Appelman HD, Beer DG, Madiyal C, Khodadost M, Nofz K, et al. Use of Appropriate Surveillance for Patients With Nondysplastic Barrett's Esophagus. Clin Gastroenterol Hepatol. 2018;16(6):862-9.e3.PMC5962402 10.1016/j.cgh.2018.01.052
137. Shaukat A, Kahi CJ, Burke CA, Rabeneck L, Sauer BG, Rex DK. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol. 2021;116(3):458-7910.14309/ajg.0000000000001122
138. Huang YK, Yu JC, Kang WM, Ma ZQ, Ye X, Tian SB, et al. Significance of Serum Pepsinogens as a Biomarker for Gastric Cancer and Atrophic Gastritis Screening: A Systematic Review and Meta-Analysis. PLoS One. 2015;10(11):e0142080.PMC4640555 10.1371/journal.pone.0142080
139. Bang CS, Lee JJ, Baik GH. Prediction of Chronic Atrophic Gastritis and Gastric Neoplasms by Serum Pepsinogen Assay: A Systematic Review and Meta-Analysis of Diagnostic Test Accuracy. J Clin Med. 2019;8(5).PMC6572271 10.3390/jcm8050657
140. Zagari RM, Rabitti S, Greenwood DC, Eusebi LH, Vestito A, Bazzoli F. Systematic review with meta-analysis: diagnostic performance of the combination of pepsinogen, gastrin-17 and anti-Helicobacter pylori antibodies serum assays for the diagnosis of atrophic gastritis. Aliment Pharmacol Ther. 2017;46(7):657-6710.1111/apt.14248
141. Kotzev AI, Draganov PV. Carbohydrate Antigen 19-9, Carcinoembryonic Antigen, and Carbohydrate Antigen 72-4 in Gastric Cancer: Is the Old Band Still Playing? Gastrointest Tumors. 2018;5(1-2):1-13.PMC6288632 10.1159/000488240
142. Shen M, Wang H, Wei K, Zhang J, You C. Five common tumor biomarkers and CEA for diagnosing early gastric cancer: A protocol for a network meta-analysis of diagnostic test accuracy. Medicine (Baltimore). 2018;97(19):e0577.PMC5959440 10.1097/md.0000000000010577
143. Dinis-Ribeiro M, Yamaki G, Miki K, Costa-Pereira A, Matsukawa M, Kurihara M. Meta-analysis on the validity of pepsinogen test for gastric carcinoma, dysplasia or chronic atrophic gastritis screening. J Med Screen. 2004;11(3):141-710.1258/0969141041732184
144. Kishino T, Oyama T, Tomori A, Takahashi A, Shinohara T. Usefulness and Limitations of a Serum Screening System to Predict the Risk of Gastric Cancer. Intern Med. 2020;59(12):1473-80.PMC7364258 10.2169/internalmedicine.3521-19

145. Kang HM, Kim GH, Jeon HK, Kim DH, Jeon TY, Park DY, et al. Circulating tumor cells detected by lab-on-a-disc: Role in early diagnosis of gastric cancer. PLoS One. 2017;12(6):e0180251.PMC5491173 10.1371/journal.pone.0180251
146. Zhou J, Ma X, Bi F, Liu M. Clinical significance of circulating tumor cells in gastric cancer patients. Oncotarget. 2017;8(15):25713-20.PMC5421964 10.18632/oncotarget.14879
147. Yamamoto H, Watanabe Y, Sato Y, Maehata T, Itoh F. Non-Invasive Early Molecular Detection of Gastric Cancers. Cancers (Basel). 2020;12(10).PMC7600616 10.3390/cancers12102880
148. Kaminski MF, Robertson DJ, Senore C, Rex DK. Optimizing the Quality of Colorectal Cancer Screening Worldwide. Gastroenterology. 2020;158(2):404-1710.1053/j.gastro.2019.11.026
149. Cusumano VT, May FP. Making FIT Count: Maximizing Appropriate Use of the Fecal Immunochemical Test for Colorectal Cancer Screening Programs. J Gen Intern Med. 2020;35(6):1870-4.PMC7280423 10.1007/s11606-020-05728-y
150. Spada C, Hassan C, Bellini D, Burling D, Cappello G, Carretero C, et al. Imaging alternatives to colonoscopy: CT colonography and colon capsule. European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) Guideline - Update 2020. Endoscopy. 2020;52(12):1127-4110.1055/a-1258-4819
151. Iyer PG, Taylor WR, Johnson ML, Lansing RL, Maixner KA, Yab TC, et al. Highly Discriminant Methylated DNA Markers for the Non-endoscopic Detection of Barrett's Esophagus. Am J Gastroenterol. 2018;113(8):1156-6610.1038/s41395-018-0107-7
152. Wartak A, Kelada AK, Leon Alarcon PA, Bablouzian AL, Ahsen OO, Gregg AL, et al. Dual-modality optical coherence tomography and fluorescence tethered capsule endomicroscopy. Biomed Opt Express. 2021;12(7):4308-23.PMC8367220 OCT-NIRS 10.1364/boe.422453
153. Krishna Chandar A, Sharma A, Chak A. Novel Screening Alternatives for Barrett Esophagus. Gastroenterol Hepatol (N Y). 2020;16(5):238-45.PMC8132638
154. Gora MJ, Quénéhervé L, Carruth RW, Lu W, Rosenberg M, Sauk JS, et al. Tethered capsule endomicroscopy for microscopic imaging of the esophagus, stomach, and duodenum without sedation in humans (with video). Gastrointest Endosc. 2018;88(5):830-40.e3.PMC8176642 10.1016/j.gie.2018.07.009
155. Alshelleh M, Inamdar S, McKinley M, Stewart M, Novak JS, Greenberg RE, et al. Incremental yield of dysplasia detection in Barrett's esophagus using volumetric laser endomicroscopy with and without laser marking compared with a standardized random biopsy protocol. Gastrointest Endosc. 2018;88(1):35-4210.1016/j.gie.2018.01.032
156. Codipilly DC, Qin Y, Dawsey SM, Kisiel J, Topazian M, Ahlquist D, et al. Screening for esophageal squamous cell carcinoma: recent advances. Gastrointest Endosc. 2018;88(3):413-26.PMC7493990 10.1016/j.gie.2018.04.2352
157. Kadri S, Lao-Sirieix P, Fitzgerald RC. Developing a nonendoscopic screening test for Barrett's esophagus. Biomark Med. 2011;5(3):397-40410.2217/bmm.11.40
158. Shariff MK, Varghese S, O'Donovan M, Abdullahi Z, Liu X, Fitzgerald RC, et al. Pilot randomized crossover study comparing the efficacy of transnasal disposable endosheath with standard endoscopy to detect Barrett's esophagus. Endoscopy. 2016;48(2):110-6.PMC6055986 10.1055/s-0034-1393310
159. Bell MG, Iyer PG. Innovations in Screening Tools for Barrett's Esophagus and Esophageal Adenocarcinoma. Curr Gastroenterol Rep. 2021;23(12):2210.1007/s11894-021-00821-6
160. Tan WK, Sharma AN, Chak A, Fitzgerald RC. Progress in Screening for Barrett's Esophagus: Beyond Standard Upper Endoscopy. Gastrointest Endosc Clin N Am. 2021;31(1):43-5810.1016/j.giec.2020.08.004
161. Clarke GA, Jacobson BC, Hammett RJ, Carr-Locke DL. The indications, utilization and safety of gastrointestinal endoscopy in an extremely elderly patient cohort. Endoscopy. 2001;33(7):580-410.1055/s-2001-15313
162. Miyanaga R, Hosoe N, Naganuma M, Hirata K, Fukuhara S, Nakazato Y, et al. Complications and outcomes of routine endoscopy in the very elderly. Endosc Int Open. 2018;6(2):E224-e9.PMC5802997 10.1055/s-0043-120569
163. Hvid-Jensen F, Pedersen L, Drewes AM, Sørensen HT, Funch-Jensen P. Incidence of adenocarcinoma among patients with Barrett's esophagus. N Engl J Med. 2011;365(15):1375-8310.1056/NEJMoa1103042
164. Killcoyne S, Fitzgerald RC. Evolution and progression of Barrett's oesophagus to oesophageal cancer. Nat Rev Cancer. 2021;21(11):731-4110.1038/s41568-021-00400-x
165. Weusten B, Bisschops R, Coron E, Dinis-Ribeiro M, Dumonceau JM, Esteban JM, et al. Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2017;49(2):191-810.1055/s-0042-122140
166. Sharma P, Shaheen NJ, Katzka D, Bergman J. AGA Clinical Practice Update on Endoscopic Treatment of Barrett's Esophagus With Dysplasia and/or Early Cancer: Expert Review. Gastroenterology. 2020;158(3):760-910.1053/j.gastro.2019.09.051
167. Zeki SS, Bergman JJ, Dunn JM. Endoscopic management of dysplasia and early oesophageal cancer. Best Pract Res Clin Gastroenterol. 2018;36-37:27-3610.1016/j.bpg.2018.11.003
168. Wei WQ, Chen ZF, He YT, Feng H, Hou J, Lin DM, et al. Long-Term Follow-Up of a Community Assignment, One-Time Endoscopic Screening Study of Esophageal Cancer in China. J Clin Oncol. 2015;33(17):1951-7.PMC4881309 online at www.jco.org. Author contributions are found at the end of this article. 10.1200/jco.2014.58.0423

169. Zhang N, Li Y, Chang X, Lei F, Ma H, Liu J, et al. Long-term effectiveness of one-time endoscopic screening for esophageal cancer: A community-based study in rural China. Cancer. 2020;126(20):4511-2010.1002/cncr.33119
170. Liu Z, Guo C, He Y, Chen Y, Ji P, Fang Z, et al. A clinical model predicting the risk of esophageal high-grade lesions in opportunistic screening: a multicenter real-world study in China. Gastrointest Endosc. 2020;91(6):1253-60.e310.1016/j.gie.2019.12.038
171. Yang F, Ma D, Li Z. Screening for esophageal squamous cell carcinoma: insight from experience with Barrett's esophagus. Gastrointest Endosc. 2019;89(2):443-4.e110.1016/j.gie.2018.09.019
172. van de Ven SEM, de Graaf W, Bugter O, Spaander MCW, Nikkessen S, de Jonge PJF, et al. Screening for synchronous esophageal second primary tumors in patients with head and neck cancer. Dis Esophagus. 2021;34(10).PMC8503417 10.1093/dote/doab037
173. Hamashima C. Update version of the Japanese Guidelines for Gastric Cancer Screening. Jpn J Clin Oncol. 2018;48(7):673-8310.1093/jjco/hyy077
174. Kim BJ, Heo C, Kim BK, Kim JY, Kim JG. Effectiveness of gastric cancer screening programs in South Korea: organized vs opportunistic models. World J Gastroenterol. 2013;19(5):736-41.PMC3574600 10.3748/wjg.v19.i5.736
175. Leja M, You W, Camargo MC, Saito H. Implementation of gastric cancer screening - the global experience. Best Pract Res Clin Gastroenterol. 2014;28(6):1093-106.PMC5847270 10.1016/j.bpg.2014.09.005
176. Zhang X, Li M, Chen S, Hu J, Guo Q, Liu R, et al. Endoscopic Screening in Asian Countries Is Associated With Reduced Gastric Cancer Mortality: A Meta-analysis and Systematic Review. Gastroenterology. 2018;155(2):347-54.e910.1053/j.gastro.2018.04.026
177. Correa P. Human gastric carcinogenesis: a multistep and multifactorial process--First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. Cancer Res. 1992;52(24):6735-40
178. Carneiro F, Machado JC, David L, Reis C, Nogueira AM, Sobrinho-Simões M. Current thoughts on the histopathogenesis of gastric cancer. Eur J Cancer Prev. 2001;10(1):101-210.1097/00008469-200102000-00013
179. Kuipers EJ, Siersema PD. The aetiology and clinical relevance of gastric intestinal metaplasia. Dig Liver Dis. 2004;36(8):501-410.1016/j.dld.2004.03.009
180. Kim GH, Liang PS, Bang SJ, Hwang JH. Screening and surveillance for gastric cancer in the United States: Is it needed? Gastrointest Endosc. 2016;84(1):18-2810.1016/j.gie.2016.02.028
181. Shah SC, Canakis A, Peek RM, Jr., Saumoy M. Endoscopy for Gastric Cancer Screening Is Cost Effective for Asian Americans in the United States. Clin Gastroenterol Hepatol. 2020;18(13):3026-39.PMC8240027 10.1016/j.cgh.2020.07.031
182. Areia M, Spaander MC, Kuipers EJ, Dinis-Ribeiro M. Endoscopic screening for gastric cancer: A cost-utility analysis for countries with an intermediate gastric cancer risk. United European Gastroenterol J. 2018;6(2):192-202.PMC5833230 10.1177/2050640617722902
183. Shichijo S, Hirata Y, Niikura R, Hayakawa Y, Yamada A, Ushiku T, et al. Histologic intestinal metaplasia and endoscopic atrophy are predictors of gastric cancer development after Helicobacter pylori eradication. Gastrointest Endosc. 2016;84(4):618-2410.1016/j.gie.2016.03.791
184. de Vries AC, van Grieken NC, Looman CW, Casparie MK, de Vries E, Meijer GA, et al. Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands. Gastroenterology. 2008;134(4):945-5210.1053/j.gastro.2008.01.071
185. Lahner E, Esposito G, Pilozzi E, Purchiaroni F, Corleto VD, Di Giulio E, et al. Occurrence of gastric cancer and carcinoids in atrophic gastritis during prospective long-term follow up. Scand J Gastroenterol. 2015;50(7):856-6510.3109/00365521.2015.1010570
186. Shah SC, Piazuelo MB, Kuipers EJ, Li D. AGA Clinical Practice Update on the Diagnosis and Management of Atrophic Gastritis: Expert Review. Gastroenterology. 2021;161(4):1325-32.e710.1053/j.gastro.2021.06.078
187. Cho SJ, Choi IJ, Kook MC, Nam BH, Kim CG, Lee JY, et al. Staging of intestinal- and diffuse-type gastric cancers with the OLGA and OLGIM staging systems. Aliment Pharmacol Ther. 2013;38(10):1292-30210.1111/apt.12515
188. Wei N, Zhou M, Lei S, Zhong Z, Shi R. A meta-analysis and systematic review on subtypes of gastric intestinal metaplasia and neoplasia risk. Cancer Cell Int. 2021;21(1):173.PMC7968216 10.1186/s12935-021-01869-0
189. Laszkowska M, Truong H, Faye AS, Kim J, Tan SX, Lim F, et al. Prevalence of Extensive and Limited Gastric Intestinal Metaplasia and Progression to Dysplasia and Gastric Cancer. Dig Dis Sci. 202110.1007/s10620-021-07276-9
190. Song H, Ekheden IG, Zheng Z, Ericsson J, Nyrén O, Ye W. Incidence of gastric cancer among patients with gastric precancerous lesions: observational cohort study in a low risk Western population. Bmj. 2015;351:h3867.PMC4516137 10.1136/bmj.h3867
191. Pimentel-Nunes P, Libânio D, Marcos-Pinto R, Areia M, Leja M, Esposito G, et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy. 2019;51(4):365-8810.1055/a-0859-1883

192. Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med. 1993;329(27):1977-8110.1056/nejm199312303292701
193. Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med. 2012;366(8):687-96.PMC3322371 10.1056/NEJMoa1100370
194. Saini SD. Colonoscopy with polypectomy reduces colorectal cancer mortality in patients with adenomas. Gastroenterology. 2012;143(4):1112-310.1053/j.gastro.2012.08.018
195. Senore C, Basu P, Anttila A, Ponti A, Tomatis M, Vale DB, et al. Performance of colorectal cancer screening in the European Union Member States: data from the second European screening report. Gut. 2019;68(7):1232-4410.1136/gutjnl-2018-317293
196. Brenner H, Stock C, Hoffmeister M. Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies. Bmj. 2014;348:g2467.PMC3980789. 10.1136/bmj.g2467
197. Cardoso R, Guo F, Heisser T, Hackl M, Ihle P, De Schutter H, et al. Colorectal cancer incidence, mortality, and stage distribution in European countries in the colorectal cancer screening era: an international population-based study. Lancet Oncol. 2021;22(7):1002-1310.1016/s1470-2045(21)00199-6
198. Grobbee EJ, van der Vlugt M, van Vuuren AJ, Stroobants AK, Mallant-Hent RC, Lansdorp-Vogelaar I, et al. Diagnostic Yield of One-Time Colonoscopy vs One-Time Flexible Sigmoidoscopy vs Multiple Rounds of Mailed Fecal Immunohistochemical Tests in Colorectal Cancer Screening. Clin Gastroenterol Hepatol. 2020;18(3):667-75.e110.1016/j.cgh.2019.08.015
199. Zhang J, Cheng Z, Ma Y, He C, Lu Y, Zhao Y, et al. Effectiveness of Screening Modalities in Colorectal Cancer: A Network Meta-Analysis. Clin Colorectal Cancer. 2017;16(4):252-6310.1016/j.clcc.2017.03.018
200. Tangka FKL, Subramanian S, Hoover S, DeGroff A, Joseph D, Wong FL, et al. Economic Evaluation of Interventions to Increase Colorectal Cancer Screening at Federally Qualified Health Centers. Health Promot Pract. 2020;21(6):877-83.PMC7894064 10.1177/1524839920954168
201. Lansdorp-Vogelaar I, Knudsen AB, Brenner H. Cost-effectiveness of colorectal cancer screening - an overview. Best Pract Res Clin Gastroenterol. 2010;24(4):439-49.PMC2939039 10.1016/j.bpg.2010.04.004
202. Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. Jama. 2021;325(19):1965-7710.1001/jama.2021.6238
203. Issa IA, Noureddine M. Colorectal cancer screening: An updated review of the available options. World J Gastroenterol. 2017;23(28):5086-96.PMC5537177 10.3748/wjg.v23.i28.5086
204. Navarro M, Nicolas A, Ferrandez A, Lanas A. Colorectal cancer population screening programs worldwide in 2016: An update. World J Gastroenterol. 2017;23(20):3632-42.PMC5449420 10.3748/wjg.v23.i20.3632
205. Altobelli E, Lattanzi A, Paduano R, Varassi G, di Orio F. Colorectal cancer prevention in Europe: burden of disease and status of screening programs. Prev Med. 2014;62:132-4110.1016/j.ypmed.2014.02.010
206. Schliemann D, Ramanathan K, Matovu N, O'Neill C, Kee F, Su TT, et al. The implementation of colorectal cancer screening interventions in low-and middle-income countries: a scoping review. BMC Cancer. 2021;21(1):112510.1186/s12885-021-08809-1
207. Hassan C, Antonelli G, Dumonceau JM, Regula J, Bretthauer M, Chaussade S, et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2020. Endoscopy. 2020;52(8):687-70010.1055/a-1185-3109
208. Gupta S, Lieberman D, Anderson JC, Burke CA, Dominitz JA, Kaltenbach T, et al. Recommendations for Follow-Up After Colonoscopy and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology. 2020;158(4):1131-53.e5.PMC7672705 10.1053/j.gastro.2019.10.026
209. van Leerdam ME, Roos VH, van Hooft JE, Balaguer F, Dekker E, Kaminski MF, et al. Endoscopic management of Lynch syndrome and of familial risk of colorectal cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2019;51(11):1082-9310.1055/a-1016-4977
210. Laine L, Kaltenbach T, Barkun A, McQuaid KR, Subramanian V, Soetikno R. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastroenterology. 2015;148(3):639-51.e2810.1053/j.gastro.2015.01.031
211. Annese V, Daperno M, Rutter MD, Amiot A, Bossuyt P, East J, et al. European evidence based consensus for endoscopy in inflammatory bowel disease. J Crohns Colitis. 2013;7(12):982-101810.1016/j.crohns.2013.09.016
212. Ianiro G, Gasbarrini A. Gastroenterology training in Europe: unmet educational needs beyond the machines. Gut. 2016;65(1):185-710.1136/gutjnl-2015-309535
213. Kaltenbach T, Anderson JC, Burke CA, Dominitz JA, Gupta S, Lieberman D, et al. Endoscopic Removal of Colorectal Lesions-Recommendations by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology. 2020;158(4):1095-12910.1053/j.gastro.2019.12.018
214. Draganov PV, Wang AY, Othman MO, Fukami N. AGA Institute Clinical Practice Update: Endoscopic Submucosal Dissection in the United States. Clin Gastroenterol Hepatol. 2019;17(1):16-25.e110.1016/j.cgh.2018.07.041
215. 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(3):270-9710.1055/s-0043-102569

216. Komeda Y, Bruno M, Koch A. EMR is not inferior to ESD for early Barrett's and EGJ neoplasia: An extensive review on outcome, recurrence and complication rates. Endoscopy international open. 2014;2(2):E58-64.4423274 10.1055/s-0034-1365528
217. van Vilsteren FG, Pouw RE, Herrero LA, Peters FP, Bisschops R, Houben M, et al. Learning to perform endoscopic resection of esophageal neoplasia is associated with significant complications even within a structured training program. Endoscopy. 2012;44(1):4-1210.1055/s-0031-1291384
218. Dolan RD, Bazarbashi AN, McCarty TR, Thompson CC, Aihara H. Endoscopic full-thickness resection of colorectal lesions: a systematic review and meta-analysis. Gastrointest Endosc. 202110.1016/j.gie.2021.09.039
219. Tweed T, van Eijden Y, Tegels J, Brenkman H, Ruurda J, van Hillegersberg R, et al. Safety and efficacy of early oral feeding for enhanced recovery following gastrectomy for gastric cancer: A systematic review. Surg Oncol. 2019;28:88-9510.1016/j.suronc.2018.11.017
220. Gu L, Khadaroo PA, Chen L, Li X, Zhu H, Zhong X, et al. Comparison of Long-Term Outcomes of Endoscopic Submucosal Dissection and Surgery for Early Gastric Cancer: a Systematic Review and Meta-analysis. J Gastrointest Surg. 2019;23(7):1493-50110.1007/s11605-019-04227-8
221. Abdelfatah MM, Barakat M, Ahmad D, Ibrahim M, Ahmed Y, Kurdi Y, et al. Long-term outcomes of endoscopic submucosal dissection versus surgery in early gastric cancer: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2019;31(4):418-2410.1097/meg.0000000000001352
222. Toyonaga T, Nishino E, Man IM, East JE, Azuma T. Principles of quality controlled endoscopic submucosal dissection with appropriate dissection level and high quality resected specimen. Clinical endoscopy. 2012;45(4):362-74.Pmc3521937 10.5946/ce.2012.45.4.362
223. Kakushima N, Fujishiro M. Endoscopic submucosal dissection for gastrointestinal neoplasms. World journal of gastroenterology. 2008;14(19):2962-7.Pmc2712159
224. Nakamoto S, Sakai Y, Kasanuki J, Kondo F, Ooka Y, Kato K, et al. Indications for the use of endoscopic mucosal resection for early gastric cancer in Japan: a comparative study with endoscopic submucosal dissection. Endoscopy. 2009;41(9):746-5010.1055/s-0029-1215010
225. Lee EJ, Lee JB, Lee SH, Youk EG. Endoscopic treatment of large colorectal tumors: comparison of endoscopic mucosal resection, endoscopic mucosal resection-precutting, and endoscopic submucosal dissection. Surgical endoscopy. 2012;26(8):2220-3010.1007/s00464-012-2164-0
226. Saito Y, Fukuzawa M, Matsuda T, Fukunaga S, Sakamoto T, Uraoka T, et al. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. Surgical endoscopy. 2010;24(2):343-5210.1007/s00464-009-0562-8
227. Yoshinaga S, Gotoda T, Kusano C, Oda I, Nakamura K, Takayanagi R. Clinical impact of endoscopic submucosal dissection for superficial adenocarcinoma located at the esophagogastric junction. Gastrointestinal endoscopy. 2008;67(2):202-910.1016/j.gie.2007.09.054
228. Oka S, Tanaka S, Kaneko I, Mouri R, Hirata M, Kawamura T, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. Gastrointest Endosc. 2006;64(6):877-8310.1016/j.gie.2006.03.932
229. Yoshida N, Wakabayashi N, Kanemasa K, Sumida Y, Hasegawa D, Inoue K, et al. Endoscopic submucosal dissection for colorectal tumors: technical difficulties and rate of perforation. Endoscopy. 2009;41(9):758-6110.1055/s-0029-1215028
230. Moss A, Bourke MJ, Williams SJ, Hourigan LF, Brown G, Tam W, et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology. 2011;140(7):1909-1810.1053/j.gastro.2011.02.062
231. Choi IJ, Kim CG, Chang HJ, Kim SG, Kook MC, Bae JM. The learning curve for EMR with circumferential mucosal incision in treating intramucosal gastric neoplasm. Gastrointestinal endoscopy. 2005;62(6):860-510.1016/j.gie.2005.04.033
232. Pimentel-Nunes P, Pioche M, Albéniz 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(10):980-9210.1055/a-0996-0912
233. Dekker E, Houwen B, Puig I, Bustamante-Balén M, Coron E, Dobru DE, et al. Curriculum for optical diagnosis training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2020;52(10):899-92310.1055/a-1231-5123
234. 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(13).PMC8269336 10.3390/jcm10132794
235. East JE, Vleugels JL, Roelandt P, Bhandari P, Bisschops R, Dekker E, et al. Advanced endoscopic imaging: European Society of Gastrointestinal Endoscopy (ESGE) Technology Review. Endoscopy. 2016;48(11):1029-4510.1055/s-0042-118087
236. Yao K, Uedo N, Kamada T, Hirasawa T, Nagahama T, Yoshinaga S, et al. Guidelines for endoscopic diagnosis of early gastric cancer. Dig Endosc. 2020;32(5):663-9810.1111/den.13684
237. Fung TLD, Chow CWS, Chan PT, Kwok KH. Review on colorectal endoscopic submucosal dissection focusing on the technical aspect. Surg Endosc. 2020;34(9):3766-8710.1007/s00464-020-07599-0
238. Saito Y, Sylvia Wu SY, Ego M, Abe S. Colorectal endoscopic submucosal dissection with use of a bipolar and insulated tip knife. VideoGIE. 2019;4(7):314-8.PMC6620361 10.1016/j.vgie.2019.04.019
239. Tsuji Y, Ohata K, Sekiguchi M, Ito T, Chiba H, Gunji T, et al. An effective training system for endoscopic submucosal dissection of gastric neoplasm. Endoscopy. 2011;43(12):1033-810.1055/s-0031-1291383

240. Aihara H, Dacha S, Anand GS, Byrne KR, Chahal P, James T, et al. Core curriculum for endoscopic submucosal dissection (ESD). Gastrointest Endosc. 2021;93(6):1215-2110.1016/j.gie.2021.01.026
241. Goda K, Fujishiro M, Hirasawa K, Kakushima N, Morita Y, Oda I, et al. How to teach and learn endoscopic submucosal dissection for upper gastrointestinal neoplasm in Japan. Dig Endosc. 2012;24 Suppl 1:136-4210.1111/j.1443-1661.2012.01274.x
242. Allum W, Lordick F, Alsina M, Andritsch E, Ba-Ssalamah A, Beishon M, et al. ECCO essential requirements for quality cancer care: Oesophageal and gastric cancer. Crit Rev Oncol Hematol. 2018;122:179-9310.1016/j.critrevonc.2017.12.019
243. Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2016;27(suppl 5):v38-v4910.1093/annonc/mdw350
244. Argilés G, Tabernero J, Labianca R, Hochhauser D, Salazar R, Iveson T, et al. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020;31(10):1291-30510.1016/j.annonc.2020.06.022
245. Vecchione L, Stintzing S, Pentheroudakis G, Douillard JY, Lordick F. ESMO management and treatment adapted recommendations in the COVID-19 era: colorectal cancer. ESMO Open. 2020;5(Suppl 3):e000826.PMC7276236 10.1136/esmoopen-2020-000826
246. Chiappa A, Andreoni B, Dionigi R, Spaggiari L, Foschi D, Polvani G, et al. A rationale multidisciplinary approach for treatment of esophageal and gastroesophageal junction cancer: Accurate review of management and perspectives. Crit Rev Oncol Hematol. 2018;132:161-810.1016/j.critrevonc.2018.10.002
247. Beets G, Sebag-Montefiore D, Andritsch E, Arnold D, Beishon M, Crul M, et al. ECCO Essential Requirements for Quality Cancer Care: Colorectal Cancer. A critical review. Crit Rev Oncol Hematol. 2017;110:81-9310.1016/j.critrevonc.2016.12.001
248. Basta YL, Bolle S, Fockens P, Tytgat K. The Value of Multidisciplinary Team Meetings for Patients with Gastrointestinal Malignancies: A Systematic Review. Ann Surg Oncol. 2017;24(9):2669-78.PMC5539280 10.1245/s10434-017-5833-3
249. Geerts PAF, van der Weijden T, Savelberg W, Altan M, Chisari G, Launert DR, et al. The Next Step Toward Patient-Centeredness in Multidisciplinary Cancer Team Meetings: An Interview Study with Professionals. J Multidiscip Healthc. 2021;14:1311-24.PMC8187002 10.2147/jmdh.S286044
250. van Huizen LS, Dijkstra PU, Hemmer PHJ, van Etten B, Buis CI, Olsder L, et al. Reorganizing the Multidisciplinary Team Meetings in a Tertiary Centre for Gastro-Intestinal Oncology Adds Value to the Internal and Regional Care Pathways. A Mixed Method Evaluation. Int J Integr Care. 2021;21(1):8.PMC7908930 10.5334/ijic.5526
251. 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(4):452-9310.1111/den.13654
252. Bourke MJ, Neuhaus H, Bergman JJ. Endoscopic Submucosal Dissection: Indications and Application in Western Endoscopy Practice. Gastroenterology. 2018;154(7):1887-900.e510.1053/j.gastro.2018.01.068
253. Ono H, Yao K, Fujishiro M, Oda I, Uedo N, Nimura S, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer (second edition). Dig Endosc. 2021;33(1):4-2010.1111/den.13883
254. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer. 2021;24(1):1-21.PMC7790804 10.1007/s10120-020-01042
255. Ishigaki T, Kudo SE, Miyachi H, Hayashi T, Minegishi Y, Toyoshima N, et al. Treatment policy for colonic laterally spreading tumors based on each clinicopathologic feature of 4 subtypes: actual status of pseudo-depressed type. Gastrointest Endosc. 2020;92(5):1083-94.e610.1016/j.gie.2020.04.033
256. Burgess NG, Hourigan LF, Zanati SA, Brown GJ, Singh R, Williams SJ, et al. Risk Stratification for Covert Invasive Cancer Among Patients Referred for Colonic Endoscopic Mucosal Resection: A Large Multicenter Cohort. Gastroenterology. 2017;153(3):732-42.e110.1053/j.gastro.2017.05.047
257. Tanaka S, Kashida H, Saito Y, Yahagi N, Yamano H, Saito S, et al. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc. 2020;32(2):219-3910.1111/den.13545
258. Han Y, Sun S, Guo J, Ge N, Wang S, Liu X, et al. Is endoscopic ultrasonography useful for endoscopic submucosal dissection? Endosc Ultrasound. 2016;5(5):284-90.PMC5070285 10.4103/2303-9027.191606
259. Parikh MP, Thota PN, Raja S, Murthy S, Ahmad U, Gupta NM, et al. Outcomes of endoscopic submucosal dissection in esophageal adenocarcinoma staged T1bN0 by endoscopic ultrasound in non-surgical patients. J Gastrointest Oncol. 2019;10(2):362-6.PMC6465506 10.21037/jgo.2018.07.12
260. Gotink AW, Spaander MCW, Doukas M, Tang TJ, Didden P, Wijnhoven BPL, et al. Exploring diagnostic and therapeutic implications of endoscopic mucosal resection in EUS-staged T2 esophageal adenocarcinoma. Endoscopy. 2017;49(10):941-810.1055/s-0043-112492
261. Chao G, Ye F, Li T, Gong W, Zhang S. Estimation of invasion depth of early colorectal cancer using EUS and NBI-ME: a meta-analysis. Tech Coloproctol. 2019;23(9):821-3010.1007/s10151-019-02076-w
262. Gall TM, Markar SR, Jackson D, Haji A, Faiz O. Mini-probe ultrasonography for the staging of colon cancer: a systematic review and meta-analysis. Colorectal Dis. 2014;16(1):O1-810.1111/codi.12445
263. van Munster S, Nieuwenhuis E, Weusten B, Alvarez Herrero L, Bogte A, Alkhalaf A, et al. Long-term outcomes after endoscopic treatment for Barrett's neoplasia with radiofrequency ablation ± endoscopic resection: results from the national Dutch database in a 10-year period. Gut. 202110.1136/gutjnl-2020-322615

264. Pech O, May A, Manner H, Behrens A, Pohl J, Weferling M, et al. Long-term efficacy and safety of endoscopic resection for patients with mucosal adenocarcinoma of the esophagus. Gastroenterology. 2014;146(3):652-60.e110.1053/j.gastro.2013.11.006
265. Phoa KN, Pouw RE, Bisschops R, Pech O, Ragunath K, Weusten BL, et al. Multimodality endoscopic eradication for neoplastic Barrett oesophagus: results of an European multicentre study (EURO-II). Gut. 2016;65(4):555-6210.1136/gutjnl-2015-309298
266. Yang D, Zou F, Xiong S, Forde JJ, Wang Y, Draganov PV. Endoscopic submucosal dissection for early Barrett's neoplasia: a meta-analysis. Gastrointest Endosc. 2018;87(6):1383-9310.1016/j.gie.2017.09.038
267. Terheggen G, Horn EM, Vieth M, Gabbert H, Enderle M, Neugebauer A, et al. A randomised trial of endoscopic submucosal dissection versus endoscopic mucosal resection for early Barrett's neoplasia. Gut. 2017;66(5):783-93.PMC5531224 10.1136/gutjnl-2015-310126
268. Mejia Perez LK, Yang D, Draganov PV, Jawaid S, Chak A, Dumot J, et al. Endoscopic submucosal dissection vs. endoscopic mucosal resection for early Barrett's neoplasia in the West: a retrospective study. Endoscopy. 202110.1055/a-1541-7659
269. Codipilly DC, Dhaliwal L, Oberoi M, Gandhi P, Johnson ML, Lansing RM, et al. Comparative Outcomes of Cap Assisted Endoscopic Resection and Endoscopic Submucosal Dissection in Dysplastic Barrett's Esophagus. Clin Gastroenterol Hepatol. 2020.PMC8128933 10.1016/j.cgh.2020.11.017
270. van de Ven SEM, Suzuki L, Gotink AW, Ten Kate FJC, Nieboer D, Weusten B, et al. Lymphovascular invasion quantification could improve risk prediction of lymph node metastases in patients with submucosal (T1b) esophageal adenocarcinoma. United European Gastroenterol J. 202110.1002/ueg2.12151
271. Manner H, Wetzka J, May A, Pauthner M, Pech O, Fisseler-Eckhoff A, et al. Early-stage adenocarcinoma of the esophagus with mid to deep submucosal invasion (pT1b sm2-3): the frequency of lymph-node metastasis depends on macroscopic and histological risk patterns. Dis Esophagus. 2017;30(3):1-1110.1111/dote.12462
272. Yamashina T, Ishihara R, Nagai K, Matsuura N, Matsui F, Ito T, et al. Long-term outcome and metastatic risk after endoscopic resection of superficial esophageal squamous cell carcinoma. Am J Gastroenterol. 2013;108(4):544-5110.1038/ajg.2013.8
273. Mizumoto T, Hiyama T, Oka S, Yorita N, Kuroki K, Kurihara M, et al. Curative Criteria After Endoscopic Resection for Superficial Esophageal Squamous Cell Carcinomas. Dig Dis Sci. 2018;63(6):1605-1210.1007/s10620-018-5029-0
274. Nagami Y, Ominami M, Shiba M, Minamino H, Fukunaga S, Kameda N, et al. The five-year survival rate after endoscopic submucosal dissection for superficial esophageal squamous cell neoplasia. Dig Liver Dis. 2017;49(4):427-3310.1016/j.dld.2016.12.009
275. Yamashina T, Ishihara R, Uedo N, Nagai K, Matsui F, Kawada N, et al. Safety and curative ability of endoscopic submucosal dissection for superficial esophageal cancers at least 50 mm in diameter. Dig Endosc. 2012;24(4):220-510.1111/j.1443-1661.2011.01215.x
276. Koterazawa Y, Nakamura T, Oshikiri T, Kanaji S, Tanaka S, Ishida T, et al. A comparison of the clinical outcomes of esophagectomy and chemoradiotherapy after noncurative endoscopic submucosal dissection for esophageal squamous cell carcinoma. Surg Today. 2018;48(8):783-9.PMC6060875 10.1007/s00595-018-1650-y
277. Takahashi K, Hashimoto S, Mizuno KI, Kobayashi T, Tominaga K, Sato H, et al. Management decision based on lymphovascular involvement leads to favorable outcomes after endoscopic treatment of esophageal squamous cell carcinoma. Endoscopy. 2018;50(7):662-7010.1055/s-0043-124433
278. Toyonaga T, Man-i M, East JE, Nishino E, Ono W, Hirooka T, et al. 1,635 Endoscopic submucosal dissection cases in the esophagus, stomach, and colorectum: complication rates and long-term outcomes. Surg Endosc. 2013;27(3):1000-8.PMC3572381 10.1007/s00464-012-2555-2
279. Repici A, Hassan C, Carlino A, Pagano N, Zullo A, Rando G, et al. Endoscopic submucosal dissection in patients with early esophageal squamous cell carcinoma: results from a prospective Western series. Gastrointest Endosc. 2010;71(4):715-2110.1016/j.gie.2009.11.020
280. Ono S, Fujishiro M, Niimi K, Goto O, Kodashima S, Yamamichi N, et al. Long-term outcomes of endoscopic submucosal dissection for superficial esophageal squamous cell neoplasms. Gastrointest Endosc. 2009;70(5):860-610.1016/j.gie.2009.04.044
281. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, et al. The 2019 WHO classification of tumours of the digestive system. Histopathology. 2020;76(2):182-8.PMC7003895 10.1111/his.13975
282. Abdelfatah MM, Barakat M, Lee H, Kim JJ, Uedo N, Grimm I, et al. The incidence of lymph node metastasis in early gastric cancer according to the expanded criteria in comparison with the absolute criteria of the Japanese Gastric Cancer Association: a systematic review of the literature and meta-analysis. Gastrointest Endosc. 2018;87(2):338-4710.1016/j.gie.2017.09.025
283. Choi KK, Bae JM, Kim SM, Sohn TS, Noh JH, Lee JH, et al. The risk of lymph node metastases in 3951 surgically resected mucosal gastric cancers: implications for endoscopic resection. Gastrointest Endosc. 2016;83(5):896-90110.1016/j.gie.2015.08.051
284. Abdelfatah MM, Barakat M, Othman MO, Grimm IS, Uedo N. The incidence of lymph node metastasis in submucosal early gastric cancer according to the expanded criteria: a systematic review. Surg Endosc. 2019;33(1):26-3210.1007/s00464-018-6451-2
285. Lian J, Chen S, Zhang Y, Qiu F. A meta-analysis of endoscopic submucosal dissection and EMR for early gastric cancer. Gastrointest Endosc. 2012;76(4):763-7010.1016/j.gie.2012.06.014

286. Tao M, Zhou X, Hu M, Pan J. Endoscopic submucosal dissection versus endoscopic mucosal resection for patients with early gastric cancer: a meta-analysis. BMJ Open. 2019;9(12):e025803.PMC7008428 10.1136/bmjopen-2018-025803
287. Park YM, Cho E, Kang HY, Kim JM. The effectiveness and safety of endoscopic submucosal dissection compared with endoscopic mucosal resection for early gastric cancer: a systematic review and metaanalysis. Surg Endosc. 2011;25(8):2666-7710.1007/s00464-011-1627-z
288. Facciorusso A, Antonino M, Di Maso M, Muscatiello N. Endoscopic submucosal dissection vs endoscopic mucosal resection for early gastric cancer: A meta-analysis. World J Gastrointest Endosc. 2014;6(11):555-63.PMC4231495 10.4253/wjge.v6.i11.555
289. Probst A, Freund S, Neuhaus L, Ebigbo A, Braun G, Goelder S, et al. Complication risk despite preventive endoscopic measures in patients undergoing endoscopic mucosal resection of large duodenal adenomas. Endoscopy. 2020;52(10):847-5510.1055/a-1144-2767
290. Navaneethan U, Hasan MK, Lourdusamy V, Zhu X, Hawes RH, Varadarajulu S. Efficacy and safety of endoscopic mucosal resection of non-ampullary duodenal polyps: a systematic review. Endosc Int Open. 2016;4(6):E699-708.PMC4993908 Shyam Varadarajulu is a consultant for Boston Scientific and Olympus. Udayakumar Navaneethan is a consultant for AbbVie, Janssen and Takeda. None of the other authors declared a financial conflict of interest. 10.1055/s-0042-107069
291. Okimoto K, Maruoka D, Matsumura T, Shiratori W, Nagashima A, Ishikawa T, et al. Long-term outcomes of cold snare polypectomy for superficial non-ampullary duodenal epithelial tumors. J Gastroenterol Hepatol. 202110.1111/jgh.15666
292. Kuroki K, Sanomura Y, Oka S, Yorita N, Kurihara M, Mizumoto T, et al. Clinical outcomes of endoscopic resection for superficial non-ampullary duodenal tumors. Endosc Int Open. 2020;8(3):E354-e9.PMC7035028 10.1055/a-0998-3708
293. Klein A, Nayyar D, Bahin FF, Qi Z, Lee E, Williams SJ, et al. Endoscopic mucosal resection of large and giant lateral spreading lesions of the duodenum: success, adverse events, and long-term outcomes. Gastrointest Endosc. 2016;84(4):688-9610.1016/j.gie.2016.02.049
294. Valerii G, Tringali A, Landi R, Boškoski I, Familiari P, Bizzotto A, et al. Endoscopic mucosal resection of non-ampullary sporadic duodenal adenomas: a retrospective analysis with long-term follow-up. Scand J Gastroenterol. 2018;53(4):490-410.1080/00365521.2018.1438508
295. Zou J, Chai N, Linghu E, Zhai Y, Li Z, Du C, et al. Clinical outcomes of endoscopic resection for non-ampullary duodenal laterally spreading tumors. Surg Endosc. 2019;33(12):4048-5610.1007/s00464-019-06698-x
296. Pérez-Cuadrado-Robles E, Quénéhervé L, Margos W, Moreels TG, Yeung R, Piessevaux H, et al. ESD versus EMR in non-ampullary superficial duodenal tumors: a systematic review and meta-analysis. Endosc Int Open. 2018;6(8):E998-e1007.PMC6075947 10.1055/a-0579-9050
297. Yahagi N, Kato M, Ochiai Y, Maehata T, Sasaki M, Kiguchi Y, et al. Outcomes of endoscopic resection for superficial duodenal epithelial neoplasia. Gastrointest Endosc. 2018;88(4):676-8210.1016/j.gie.2018.05.002
298. Hoteya S, Furuhata T, Takahito T, Fukuma Y, Suzuki Y, Kikuchi D, et al. Endoscopic Submucosal Dissection and Endoscopic Mucosal Resection for Non-Ampullary Superficial Duodenal Tumor. Digestion. 2017;95(1):36-4210.1159/000452363
299. Shibagaki K, Ishimura N, Kinoshita Y. Endoscopic submucosal dissection for duodenal tumors. Ann Transl Med. 2017;5(8):188.PMC5464942 10.21037/atm.2017.03.63
300. Vanbiervliet G, Moss A, Arvanitakis M, Arnelo U, Beyna T, Busch O, et al. Endoscopic management of superficial nonampullary duodenal tumors: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2021;53(5):522-3410.1055/a-1442-2395
301. Hassan C, Repici A, Sharma P, Correale L, Zullo A, Bretthauer M, et al. Efficacy and safety of endoscopic resection of large colorectal polyps: a systematic review and meta-analysis. Gut. 2016;65(5):806-2010.1136/gutjnl-2014-308481
302. Shahini E, Libânio D, Lo Secco G, Pisani A, Arezzo A. Indications and outcomes of endoscopic resection for non-pedunculated colorectal lesions: A narrative review. World J Gastrointest Endosc. 2021;13(8):275-95.PMC8394186 10.4253/wjge.v13.i8.275
303. Belderbos TD, Leenders M, Moons LM, Siersema PD. Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: systematic review and meta-analysis. Endoscopy. 2014;46(5):388-40210.1055/s-0034-1364970
304. Kim HG, Sethi S, Banerjee S, Friedland S. Outcomes of endoscopic treatment of second recurrences of large nonpedunculated colorectal adenomas. Surg Endosc. 2016;30(6):2457-6410.1007/s00464-015-4497-y
305. Klein A, Tate DJ, Jayasekeran V, Hourigan L, Singh R, Brown G, et al. Thermal Ablation of Mucosal Defect Margins Reduces Adenoma Recurrence After Colonic Endoscopic Mucosal Resection. Gastroenterology. 2019;156(3):604-13.e310.1053/j.gastro.2018.10.003
306. Tate DJ, Desomer L, Klein A, Brown G, Hourigan LF, Lee EY, et al. Adenoma recurrence after piecemeal colonic EMR is predictable: the Sydney EMR recurrence tool. Gastrointest Endosc. 2017;85(3):647-56.e610.1016/j.gie.2016.11.027
307. Moss A, Williams SJ, Hourigan LF, Brown G, Tam W, Singh R, et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut. 2015;64(1):57-6510.1136/gutjnl-2013-305516

308. Awadie H, Repici A, Bourke MJ. Endoscopic management of large nonpedunculated colorectal polyps: selective treatment algorithms are needed. Endoscopy. 2017;49(3):214-610.1055/s-0043-102491
309. 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(8):670-610.1055/s-0034-1365810
310. Ericsson KA. Acquisition and maintenance of medical expertise: a perspective from the expert-performance approach with deliberate practice. Acad Med. 2015;90(11):1471-8610.1097/acm.0000000000000939
311. van Merriënboer JJ, Sweller J. Cognitive load theory in health professional education: design principles and strategies. Med Educ. 2010;44(1):85-9310.1111/j.1365-2923.2009.03498.x
312. Mehdi Z, Ross A, Reedy G, Roots A, Ernst T, Jaye P, et al. Simulation training for geriatric medicine. Clin Teach. 2014;11(5):387-9210.1111/tct.12156
313. Lioce L. (Ed.) LJFE, Downing D., Chang T.P., Robertson J.M., Anderson M., Diaz D.A., and Spain A.E. (Assoc. Eds.). Healthcare Simulation Dictionary. 2nd ed: Agency for Healthcare Research and Quality; 2020.
314. Cook DA, Hatala R, Brydges R, Zendejas B, Szostek JH, Wang AT, et al. Technology-enhanced simulation for health professions education: a systematic review and meta-analysis. Jama. 2011;306(9):978-8810.1001/jama.2011.1234
315. Kronschnabl DM, Baerwald C, Rotzoll DE. Evaluating the effectiveness of a structured, simulator-assisted, peer-led training on cardiovascular physical examination in third-year medical students: a prospective, randomized, controlled trial. GMS J Med Educ. 2021;38(6):Doc108.PMC8493837 10.3205/zma001504
316. Boet S, Bould MD, Fung L, Qosa H, Perrier L, Tavares W, et al. Transfer of learning and patient outcome in simulated crisis resource management: a systematic review. Can J Anaesth. 2014;61(6):571-82.PMC4028539 10.1007/s12630-014-0143-8
317. Sinclair P, Kable A, Levett-Jones T. The effectiveness of internet-based e-learning on clinician behavior and patient outcomes: a systematic review protocol. JBI Database System Rev Implement Rep. 2015;13(1):52-6410.11124/jbisrir-2015-1919
318. Cook DA, Brydges R, Zendejas B, Hamstra SJ, Hatala R. Mastery learning for health professionals using technology-enhanced simulation: a systematic review and meta-analysis. Acad Med. 2013;88(8):1178-8610.1097/ACM.0b013e31829a365d
319. Cheng A, Kessler D, Mackinnon R, Chang TP, Nadkarni VM, Hunt EA, et al. Reporting Guidelines for Health Care Simulation Research: Extensions to the CONSORT and STROBE Statements. Simul Healthc. 2016;11(4):238-4810.1097/sih.0000000000000150
320. Brydges R, Hatala R, Zendejas B, Erwin PJ, Cook DA. Linking simulation-based educational assessments and patient-related outcomes: a systematic review and meta-analysis. Acad Med. 2015;90(2):246-5610.1097/acm.0000000000000549
321. Cheng A, Grant V, Auerbach M. Using simulation to improve patient safety: dawn of a new era. JAMA Pediatr. 2015;169(5):419-2010.1001/jamapediatrics.2014.3817
322. Lei C, Palm K. Crisis Resource Management Training in Medical Simulation. StatPearls. Treasure Island (FL): StatPearls Publishing. Copyright © 2021, StatPearls Publishing LLC.; 2021.
323. Palaganas JC, Epps C, Raemer DB. A history of simulation-enhanced interprofessional education. J Interprof Care. 2014;28(2):110-510.3109/13561820.2013.869198
324. Steinert Y, Naismith L, Mann K. Faculty development initiatives designed to promote leadership in medical education. A BEME systematic review: BEME Guide No. 19. Med Teach. 2012;34(6):483-50310.3109/0142159x.2012.680937
325. Pietersen PI, Bjerrum F, Tolsgaard MG, Konge L, Andersen SAW. Standard Setting in Simulation-Based Training of Surgical Procedures: A Systematic Review. Ann Surg. 2021.10.1097/sla.0000000000005209
326. Dobalian A, Bowman CC, Wyte-Lake T, Pearson ML, Dougherty MB, Needleman J. The critical elements of effective academic-practice partnerships: a framework derived from the Department of Veterans Affairs Nursing Academy. BMC Nurs. 2014;13(1):183.PMC4279967 10.1186/s12912-014-0036-8
327. Girotto LC, Enns SC, de Oliveira MS, Mayer FB, Perotta B, Santos IS, et al. Preceptors' perception of their role as educators and professionals in a health system. BMC Med Educ. 2019;19(1):203.PMC6567907 10.1186/s12909-019-1642-7
328. Blero D, Devière J. Endoscopic complications--avoidance and management. Nat Rev Gastroenterol Hepatol. 2012;9(3):162-7210.1038/nrgastro.2012.3
329. Razavi F, Gross S, Katz S. Endoscopy in the elderly: risks, benefits, and yield of common endoscopic procedures. Clin Geriatr Med. 2014;30(1):133-4710.1016/j.cger.2013.10.010
330. Walsh CM, Ling SC, Khanna N, Grover SC, Yu JJ, Cooper MA, et al. Gastrointestinal Endoscopy Competency Assessment Tool: reliability and validity evidence. Gastrointest Endosc. 2015;81(6):1417-24.e210.1016/j.gie.2014.11.030
331. Khan R, Scaffidi MA, Grover SC, Gimpaya N, Walsh CM. Simulation in endoscopy: Practical educational strategies to improve learning. World J Gastrointest Endosc. 2019;11(3):209-18.PMC6425285 10.4253/wjge.v11.i3.209
332. Goodman AJ, Melson J, Aslanian HR, Bhutani MS, Krishnan K, Lichtenstein DR, et al. Endoscopic simulators. Gastrointest Endosc. 2019;90(1):1-1210.1016/j.gie.2018.10.037
333. Dolan RD, Ryou M. Endoscopic simulators: training the next generation. Curr Opin Gastroenterol. 2021;37(6):589-9510.1097/mog.0000000000000788

334. Hochberger J, Maiss J, Magdeburg B, Cohen J, Hahn EG. Training simulators and education in gastrointestinal endoscopy: current status and perspectives in 2001. Endoscopy. 2001;33(6):541-910.1055/s-2001-14972
335. Sedlack R, Petersen B, Binmoeller K, Kolars J. A direct comparison of ERCP teaching models. Gastrointestinal endoscopy. 2003;57(7):886-9010.1067/mge.2003.236
336. Sedlack RE, Kolars JC. Computer simulator training enhances the competency of gastroenterology fellows at colonoscopy: results of a pilot study. Am J Gastroenterol. 2004;99(1):33-710.1111/j.1572-0241.2004.04007.x
337. Koch AD, Ekkelenkamp VE, Haringsma J, Schoon EJ, de Man RA, Kuipers EJ. Simulated colonoscopy training leads to improved performance during patient-based assessment. Gastrointest Endosc. 2015;81(3):630-610.1016/j.gie.2014.09.014
338. Bhatt A, Abe S, Kumaravel A, Parsi MA, Stevens T, Jang S, et al. Video-based supervision for training of endoscopic submucosal dissection. Endoscopy. 2016;48(8):711-610.1055/s-0042-106722
339. Pioche M, Rivory J, Nishizawa T, Uraoka T, Touzet S, O'Brien M, et al. Randomized comparative evaluation of endoscopic submucosal dissection self-learning software in France and Japan. Endoscopy. 2016;48(12):1076-8310.1055/s-0042-116946
340. Kato M, Gromski M, Jung Y, Chuttani R, Matthes K. The learning curve for endoscopic submucosal dissection in an established experimental setting. Surg Endosc. 2013;27(1):154-6110.1007/s00464-012-2402-5
341. Gromski MA, Cohen J, Saito K, Gonzalez JM, Sawhney M, Kang C, et al. Learning colorectal endoscopic submucosal dissection: a prospective learning curve study using a novel ex vivo simulator. Surg Endosc. 2017;31(10):4231-710.1007/s00464-017-5484-2
342. Coda S, Trentino P, Antonellis F, Porowska B, Gossetti F, Ruberto F, et al. A Western single-center experience with endoscopic submucosal dissection for early gastrointestinal cancers. Gastric cancer : official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association. 2010;13(4):258-6310.1007/s10120-010-0544-5
343. Friedel D, Stavropoulos SN. Introduction of endoscopic submucosal dissection in the West. World J Gastrointest Endosc. 2018;10(10):225-38.PMC6198314 10.4253/wjge.v10.i10.225
344. Hirasawa K, Kokawa A, Oka H, Yahara S, Sasaki T, Nozawa A, et al. Risk assessment chart for curability of early gastric cancer with endoscopic submucosal dissection. Gastrointest Endosc. 2011;74(6):1268-7510.1016/j.gie.2011.07.067
345. 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(6):1188-9610.1016/j.gie.2012.08.024
346. Yang DH, Jeong GH, Song Y, Park SH, Park SK, Kim JW, et al. The Feasibility of Performing Colorectal Endoscopic Submucosal Dissection Without Previous Experience in Performing Gastric Endoscopic Submucosal Dissection. Dig Dis Sci. 2015;60(11):3431-4110.1007/s10620-015-3755-0
347. 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(3):368-7310.1111/den.12353
348. Chong DH, Poon CM, Leong HT. Colorectal endoscopic submucosal dissection at a low-volume centre: tips and tricks, and learning curve in a district hospital in Hong Kong. Hong Kong Med J. 2016;22(3):256-6210.12809/hkmj154736
349. Shiga H, Endo K, Kuroha M, Kakuta Y, Takahashi S, Kinouchi Y, et al. Endoscopic submucosal dissection for colorectal neoplasia during the clinical learning curve. Surg Endosc. 2014;28(7):2120-810.1007/s00464-014-3443-8
350. Shiga H, Kuroha M, Endo K, Kimura T, Kakuta Y, Kinouchi Y, et al. Colorectal endoscopic submucosal dissection (ESD) performed by experienced endoscopists with limited experience in gastric ESD. Int J Colorectal Dis. 2015;30(12):1645-5210.1007/s00384-015-2334-3
351. Yang D, Wagh MS, Draganov PV. The status of training in new technologies in advanced endoscopy: from defining competence to credentialing and privileging. Gastrointest Endosc. 2020;92(5):1016-25.PMC7267783 10.1016/j.gie.2020.05.047
352. Gotoda T, Friedland S, Hamanaka H, Soetikno R. A learning curve for advanced endoscopic resection. Gastrointest Endosc. 2005;62(6):866-710.1016/j.gie.2005.07.055
353. Dinis-Ribeiro M, Pimentel-Nunes P, Afonso M, Costa N, Lopes C, Moreira-Dias L. A European case series of endoscopic submucosal dissection for gastric superficial lesions. Gastrointest Endosc. 2009;69(2):350-510.1016/j.gie.2008.08.035
354. Faulx AL, Lightdale JR, Acosta RD, Agrawal D, Bruining DH, Chandrasekhara V, et al. Guidelines for privileging, credentialing, and proctoring to perform GI endoscopy. Gastrointest Endosc. 2017;85(2):273-8110.1016/j.gie.2016.10.036
355. 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(4):302-610.1111/j.1443-1661.2010.01005.x
356. Jeon HH, Lee HS, Youn YH, Park JJ, Park H. Learning curve analysis of colorectal endoscopic submucosal dissection (ESD) for laterally spreading tumors by endoscopists experienced in gastric ESD. Surg Endosc. 2016;30(6):2422-3010.1007/s00464-015-4493-2

357. 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(10):1307-1210.1097/DCR.0b013e3182282ab0
358. Rönnow 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(11):E1340-e8.PMC6221812 10.1055/a-0733-3668
359. Rajendran A, Pannick S, Thomas-Gibson S, Oke S, Anele C, Sevdalis N, et al. Systematic literature review of learning curves for colorectal polyp resection techniques in lower gastrointestinal endoscopy. Colorectal Dis. 2020;22(9):1085-10010.1111/codi.14960
360. 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(1):74-86.e1710.1016/j.gie.2017.02.024
361. 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(23):2518-36.PMC6010943 10.3748/wjg.v24.i23.2518
362. Catalano F, Mengardo V, Trecca A, Tomezzoli A, Rodella L, Cerofolini A, et al. The impact of experience on short- and long-term outcomes on gastric ESD: a western series. Updates Surg. 2019;71(2):359-6510.1007/s13304-019-00628-1
363. Fuccio L, Bhandari P, Maselli R, Frazzoni L, Ponchon T, Bazzoli F, et al. Ten quality indicators for endoscopic submucosal dissection: what should be monitored and reported to improve quality. Ann Transl Med. 2018;6(13):262.PMC6064796 10.21037/atm.2018.05.42
364. Kotzev AI, Yang D, Draganov PV. How to master endoscopic submucosal dissection in the USA. Dig Endosc. 2019;31(1):94-10010.1111/den.13240
365. van der Wiel SE, Kuttner Magalhaes R, Rocha Goncalves CR, Dinis-Ribeiro M, Bruno MJ, Koch AD. Simulator training in gastrointestinal endoscopy - From basic training to advanced endoscopic procedures. Best Pract Res Clin Gastroenterol. 2016;30(3):375-8710.1016/j.bpg.2016.04.004
366. Kuttner-Magalhaes R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD. Training in endoscopic mucosal resection and endoscopic submucosal dissection: Face, content and expert validity of the live porcine model. United European Gastroenterol J. 2018;6(4):547-57.PMC5987272 10.1177/2050640617742484
367. Küttner Magalhães R, Dinis-Ribeiro M, Bruno MJ, Marcos-Pinto R, Rolanda C, Koch AD. A steep early learning curve for Endoscopic Submucosal Dissection (ESD) in the live porcine model. Dig Dis. 202110.1159/000521429
368. Küttner-Magalhães R, Pimentel-Nunes P, Araújo-Martins M, Libânio D, Borges-Canha M, Marcos-Pinto R, et al. Endoscopic submucosal dissection (ESD): how do Western endoscopists value animal models? Scand J Gastroenterol. 2021:1-510.1080/00365521.2021.1879251
369. Küttner Magalhães R, Dinis-Ribeiro M, Marcos-Pinto R, Rolanda C, Koch AD. Endoscopic Submucosal Dissection (ESD) skills transfer to clinical practice after hands-on workshops: an international survey. Dig Dis. 202110.1159/000521274
370. Seam N, Lee AJ, Vennero M, Emlet L. Simulation Training in the ICU. Chest. 2019;156(6):1223-33.PMC6945651 10.1016/j.chest.2019.07.011
371. Pastis NJ, Tobin CD, Wolf BJ, Reves JG, Schaefer JJ. A Pilot Study of Simulation Training in Difficult Bag Mask Ventilation Using a Computerized Patient Simulator. J Med Educ Curric Dev. 2019;6:2382120519834327.PMC6435869 10.1177/2382120519834327
372. Fransen AF, van de Ven J, Banga FR, Mol BWJ, Oei SG. Multi-professional simulation-based team training in obstetric emergencies for improving patient outcomes and trainees' performance. Cochrane Database Syst Rev. 2020;12(12):Cd011545.PMC8094450 10.1002/14651858.CD011545.pub2
373. Myer CMt, Jabbour N. Advanced Pediatric Airway Simulation. Otolaryngol Clin North Am. 2017;50(5):923-3110.1016/j.otc.2017.05.004
374. Ziv A, Wolpe PR, Small SD, Glick S. Simulation-based medical education: an ethical imperative. Simul Healthc. 2006;1(4):252-610.1097/01.Sih.0000242724.08501.63
375. Busche K, Burak KW, Veale P, Coderre S, McLaughlin K. Making progress in the ethical treatment of medical trainees. Adv Health Sci Educ Theory Pract. 2016;21(3):711-810.1007/s10459-015-9617-x
376. Cook DA, Hamstra SJ, Brydges R, Zendejas B, Szostek JH, Wang AT, et al. Comparative effectiveness of instructional design features in simulation-based education: systematic review and meta-analysis. Med Teach. 2013;35(1):e867-9810.3109/0142159x.2012.714886
377. Bradley P. The history of simulation in medical education and possible future directions. Med Educ. 2006;40(3):254-6210.1111/j.1365-2929.2006.02394.x
378. Watson K, Wright A, Morris N, McMeeken J, Rivett D, Blackstock F, et al. Can simulation replace part of clinical time? Two parallel randomised controlled trials. Med Educ. 2012;46(7):657-6710.1111/j.1365-2923.2012.04295.x
379. Martinek J, Stefanova M, Suchanek S, Zavada F, Svobodova B, Strosova A, et al. Training of different endoscopic skills on ex-vivo animal model. Simulation in healthcare : journal of the Society for Simulation in Healthcare. 2014;9(2):112-910.1097/SIH.0b013e31829be99e
380. Yoshida N, Yagi N, Inada Y, Kugai M, Kamada K, Katada K, et al. Possibility of ex vivo animal training model for colorectal endoscopic submucosal dissection. International journal of colorectal disease. 2013;28(1):49-5610.1007/s00384-012-1531-6

381. Tanimoto MA, Torres-Villalobos G, Fujita R, Santillan-Doherty P, Albores-Saavedra J, Gutierrez G, et al. Endoscopic submucosal dissection in dogs in a World Gastroenterology Organisation training center. World J Gastroenterol. 2010;16(14):1759-64.PMC2852825 10.3748/wjg.v16.i14.1759
382. David L. Streiner GRN, John Cairney. Health Measurement Scales. Fifth ed: Oxford University Press; 2015.
383. Keszei AP, Novak M, Streiner DL. Introduction to health measurement scales. Journal of psychosomatic research. 2010;68(4):319-2310.1016/j.jpsychores.2010.01.006
384. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. Journal of clinical epidemiology. 2010;63(7):737-4510.1016/j.jclinepi.2010.02.006
385. Wang TE, Wang HY, Lin CC, Chen TY, Chang CW, Chen CJ, et al. Simulating a target lesion for endoscopic submucosal dissection training in an ex vivo pig model. Gastrointestinal endoscopy. 2011;74(2):398-40210.1016/j.gie.2011.04.014
386. Horii J, Goto O, Shimoda M, Sasaki M, Fujimoto A, Ochiai Y, et al. Which part of a porcine stomach is suitable as an animal training model for gastric endoscopic submucosal dissection? Endoscopy. 2016;48(2):188-9310.1055/s-0034-1393047
387. Yamamoto S, Uedo N, Ishihara R, Kajimoto N, Ogiyama H, Fukushima Y, et al. Endoscopic submucosal dissection for early gastric cancer performed by supervised residents: assessment of feasibility and learning curve. Endoscopy. 2009;41(11):923-810.1055/s-0029-1215129
388. He Y, Fu K, Leung J, Du Y, Wang J, Jin P, et al. Traction with dental floss and endoscopic clip improves trainee success in performing gastric endoscopic submucosal dissection (ESD): a live porcine study (with video). Surg Endosc. 2016;30(7):3138-4410.1007/s00464-015-4598-7
389. Chapelle N, Musquer N, Metivier-Cesbron E, Luet D, Volteau C, Le Rhun M, et al. Efficacy of a three-day training course in endoscopic submucosal dissection using a live porcine model: a prospective evaluation. United European Gastroenterol J. 2018;6(9):1410-6.PMC6206532 10.1177/2050640618788694
390. Kasapidis P, Bassioukas S, Mavrogenis G, Tribonias G, Delis K, Georgopoulos S, et al. Experimental gastric endoscopic submucosal dissection: training in a porcine model. Ann Gastroenterol. 2017;30(4):446-9.PMC5479999 10.20524/aog.2017.0147
391. Teoh AY, Chiu PW, Wong SK, Sung JJ, Lau JY, Ng EK. Difficulties and outcomes in starting endoscopic submucosal dissection. Surg Endosc. 2010;24(5):1049-5410.1007/s00464-009-0724-8
392. Pioche M, Rivory J, Aguero-Garcete G, Guillaud O, O'Brien M, Lafon C, et al. New isolated bovine colon model dedicated to colonic ESD hands-on training: development and first evaluation. Surg Endosc. 2015;29(11):3209-1510.1007/s00464-014-4062-0
393. Fujishiro M, Jung HY, Goda K, Hirasawa K, Kakushima N, Lee IL, et al. Desirable training and roles of Japanese endoscopists towards the further penetration of endoscopic submucosal dissection in Asia. Dig Endosc. 2012;24 Suppl 1:121-310.1111/j.1443-1661.2012.01254.x
394. Lee JG, Park CH, Chung H, Park JC, Kim DH, Lee BI, et al. Current status and trend in training for endoscopic submucosal dissection: A nationwide survey in Korea. PLoS One. 2020;15(5):e0232691.PMC7209322 10.1371/journal.pone.0232691
395. Yamamoto S, Radomski T, Shafazand M. Implementation of mentor-assisted colorectal endoscopic submucosal dissection in Sweden; learning curve and clinical outcomes. Scand J Gastroenterol. 2018;53(9):1146-5210.1080/00365521.2018.1498912
396. McCarty TR, Aihara H. Current state of education and training for endoscopic submucosal dissection: Translating strategy and success to the USA. Dig Endosc. 201910.1111/den.13591
397. Jacques J, Legros R, Charissoux A, Mesturoux L, Couquet CY, Carrier P, et al. A local structured training program with live pigs allows performing ESD along the gastrointestinal tract with results close to those of Japanese experts. Dig Liver Dis. 2016;48(12):1457-6210.1016/j.dld.2016.08.111
398. Koch AD, Haringsma J, Schoon EJ, de Man RA, Kuipers EJ. Competence measurement during colonoscopy training: the use of self-assessment of performance measures. Am J Gastroenterol. 2012;107(7):971-510.1038/ajg.2011.481
399. Siau K, Green JT, Hawkes ND, Broughton R, Feeney M, Dunckley P, et al. Impact of the Joint Advisory Group on Gastrointestinal Endoscopy (JAG) on endoscopy services in the UK and beyond. Frontline Gastroenterol. 2019;10(2):93-106.PMC6540274 10.1136/flgastro-2018-100969
400. Reznick RK, MacRae H. Teaching surgical skills--changes in the wind. N Engl J Med. 2006;355(25):2664-910.1056/NEJMra054785
401. Dabbagh A, Abtahi D, Aghamohammadi H, Ahmadizadeh SN, Ardehali SH. Relationship Between "Simulated Patient Scenarios and Role-Playing" Method and OSCE Performance in Senior Anesthesiology Residents: A Correlation Assessment Study. Anesth Pain Med. 2020;10(5):e106640.PMC8207878 10.5812/aapm.106640
402. Evgeniou E, Loizou P. Simulation-based surgical education. ANZ J Surg. 2013;83(9):619-2310.1111/j.1445-2197.2012.06315.x
403. Rudolph JW, Raemer DB, Simon R. Establishing a safe container for learning in simulation: the role of the presimulation briefing. Simul Healthc. 2014;9(6):339-4910.1097/sih.0000000000000047
404. Bambini D. Writing a Simulation Scenario: A Step-By-Step Guide. AACN Adv Crit Care. 2016;27(1):62-7010.4037/aacnacc2016986

405. O'Regan S, Molloy E, Watterson L, Nestel D. Observer roles that optimise learning in healthcare simulation education: a systematic review. Adv Simul (Lond). 2016;1:4.PMC5796608 10.1186/s41077-015-0004-8
406. Morse KJ, Fey MK, Forneris SG. Evidence-Based Debriefing. Annu Rev Nurs Res. 2020;39(1):129-4810.1891/0739-6686.39.129
407. Abbott EF, Laack TA, Licatino LK, Wood-Wentz CM, Warner PA, Torsher LC, et al. Comparison of dyad versus individual simulation-based training on stress, anxiety, cognitive load, and performance: a randomized controlled trial. BMC Med Educ. 2021;21(1):367.PMC8256490 10.1186/s12909-021-02786-6
408. Thompson R, Sullivan S, Campbell K, Osman I, Statz B, Jung HS. Does a Written Tool to Guide Structured Debriefing Improve Discourse? Implications for Interprofessional Team Simulation. J Surg Educ. 2018;75(6):e240-e510.1016/j.jsurg.2018.07.001
409. Abulebda K, Srinivasan S, Maa T, Stormorken A, Chumpitazi CE. Development, Implementation, and Evaluation of a Faculty Development Workshop to Enhance Debriefing Skills Among Novice Facilitators. Cureus. 2020;12(2):e6942.PMC7071841 10.7759/cureus.6942
410. van Dalen A, Jansen M, van Haperen M, van Dieren S, Buskens CJ, Nieveen van Dijkum EJM, et al. Implementing structured team debriefing using a Black Box in the operating room: surveying team satisfaction. Surg Endosc. 2021;35(3):1406-19.PMC7886753 10.1007/s00464-020-07526-3
411. Arora S, Ahmed M, Paige J, Nestel D, Runnacles J, Hull L, et al. Objective structured assessment of debriefing: bringing science to the art of debriefing in surgery. Ann Surg. 2012;256(6):982-810.1097/SLA.0b013e3182610c91
412. Cohen J, Bosworth BP, Chak A, Dunkin BJ, Early DS, Gerson LB, et al. Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) on the use of endoscopy simulators for training and assessing skill. Gastrointest Endosc. 2012;76(3):471-510.1016/j.gie.2012.03.248
413. Ward ST, Mohammed MA, Walt R, Valori R, Ismail T, Dunckley P. An analysis of the learning curve to achieve competency at colonoscopy using the JETS database. Gut. 2014;63(11):1746-54.PMC4215302 10.1136/gutjnl-2013-305973
414. Wani S, Keswani RN, Petersen B, Edmundowicz SA, Walsh CM, Huang C, et al. Training in EUS and ERCP: standardizing methods to assess competence. Gastrointest Endosc. 2018;87(6):1371-8210.1016/j.gie.2018.02.009
415. Koch AD, Buzink SN, Heemskerk J, Botden SM, Veenendaal R, Jakimowicz JJ, et al. Expert and construct validity of the Simbionix GI Mentor II endoscopy simulator for colonoscopy. Surg Endosc. 2008;22(1):158-62.PMC2169271 10.1007/s00464-007-9394-6
416. Sedlack RE, Kolars JC. Validation of a computer-based colonoscopy simulator. Gastrointest Endosc. 2003;57(2):214-810.1067/mge.2003.81
417. Holden MS, Wang CN, MacNeil K, Church B, Hookey L, Fichtinger G, et al. Objective assessment of colonoscope manipulation skills in colonoscopy training. Int J Comput Assist Radiol Surg. 2018;13(1):105-1410.1007/s11548-017-1676-4
418. McConnell RA, Kim S, Ahmad NA, Falk GW, Forde KA, Ginsberg GG, et al. Poor discriminatory function for endoscopic skills on a computer-based simulator. Gastrointest Endosc. 2012;76(5):993-100210.1016/j.gie.2012.07.024
419. Sarker SK, Albrani T, Zaman A, Kumar I. Procedural performance in gastrointestinal endoscopy: live and simulated. World J Surg. 2010;34(8):1764-7010.1007/s00268-010-0579-0
420. Blackburn SC, Griffin SJ. Role of simulation in training the next generation of endoscopists. World J Gastrointest Endosc. 2014;6(6):234-9.PMC4055992 10.4253/wjge.v6.i6.234
421. Elvevi A, Cantù P, Maconi G, Conte D, Penagini R. Evaluation of hands-on training in colonoscopy: is a computer-based simulator useful? Dig Liver Dis. 2012;44(7):580-410.1016/j.dld.2012.03.014
422. Thompson CC, Jirapinyo P, Kumar N, Ou A, Camacho A, Lengyel B, et al. Development and initial validation of an endoscopic part-task training box. Endoscopy. 2014;46(9):735-44.PMC5019102 10.1055/s-0034-1365463
423. Tamai N, Aihara H, Kato M, Isshi K, Sumiyama K. Competency assessment for gastric endoscopic submucosal dissection using an endoscopic part-task training box. Surg Endosc. 2019;33(8):2548-5210.1007/s00464-018-6548-7
424. Ou A, Shin CM, Goodman AJ, Poles MA, Popov VB. Endoscopic part-task training box scores correlate with endoscopic outcomes. Surg Endosc. 2021;35(7):3592-910.1007/s00464-020-07830-y
425. Waschke KA, Anderson J, Valori RM, MacIntosh DG, Kolars JC, DiSario JA, et al. ASGE principles of endoscopic training. Gastrointest Endosc. 2019;90(1):27-3410.1016/j.gie.2018.10.017
426. Moorthy K, Munz Y, Orchard TR, Gould S, Rockall T, Darzi A. An innovative method for the assessment of skills in lower gastrointestinal endoscopy. Surg Endosc. 2004;18(11):1613-910.1007/s00464-004-9002-y
427. Haycock A, Koch AD, Familiari P, van Delft F, Dekker E, Petruzziello L, et al. Training and transfer of colonoscopy skills: a multinational, randomized, blinded, controlled trial of simulator versus bedside training. Gastrointest Endosc. 2010;71(2):298-30710.1016/j.gie.2009.07.017
428. Walsh CM. In-training gastrointestinal endoscopy competency assessment tools: Types of tools, validation and impact. Best Pract Res Clin Gastroenterol. 2016;30(3):357-7410.1016/j.bpg.2016.04.001
429. Bisschops R, Areia M, Coron E, Dobru D, Kaskas B, Kuvaev R, et al. Performance measures for upper gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy. 2016;48(9):843-6410.1055/s-0042-113128

430. Kaminski MF, Thomas-Gibson S, Bugajski M, Bretthauer M, Rees CJ, Dekker E, et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy. 2017;49(4):378-9710.1055/s-0043-103411
431. Domagk D, Oppong KW, Aabakken L, Czakó L, Gyökeres T, Manes G, et al. Performance measures for ERCP and endoscopic ultrasound: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy. 2018;50(11):1116-2710.1055/a-0749-8767
432. Spada C, McNamara D, Despott EJ, Adler S, Cash BD, Fernández-Urién I, et al. Performance measures for small-bowel endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy. 2019;51(6):574-9810.1055/a-0889-9586
433. Valori R, Cortas G, de Lange T, Salem Balfaqih O, de Pater M, Eisendrath P, et al. Performance measures for endoscopy services: A European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative. United European Gastroenterol J. 2019;7(1):21-44.PMC6374839 10.1177/2050640618810242
434. Bisschops R, Dinis-Ribeiro M. ESGE quality parameters in colonoscopy: How to ensure their adoption? Endosc Int Open. 2021;9(10):E1463-e5.PMC8445679 10.1055/a-1486-6788
435. Bisschops R, Rutter MD, Areia M, Spada C, Domagk D, Kaminski MF, et al. Overcoming the barriers to dissemination and implementation of quality measures for gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) and United European Gastroenterology (UEG) position statement. Endoscopy. 2021;53(2):196-20210.1055/a-1312-6389
436. Teunissen PW, Watling CJ, Schrewe B, Asgarova S, Ellaway R, Myers K, et al. Contextual Competence: How residents develop competent performance in new settings. Med Educ. 2021;55(9):1100-9.PMC8451833 10.1111/medu.14517
437. Neve H, Hanks S. When I say … capability. Med Educ. 2016;50(6):610-110.1111/medu.12956
438. Schutz SM, Abbott RM. Grading ERCPs by degree of difficulty: a new concept to produce more meaningful outcome data. Gastrointest Endosc. 2000;51(5):535-910.1016/s0016-5107(00)70285-9
439. Olsson G, Arnelo U, Swahn F, Törnqvist B, Lundell L, Enochsson L. The H.O.U.S.E. classification: a novel endoscopic retrograde cholangiopancreatography (ERCP) complexity grading scale. BMC Gastroenterol. 2017;17(1):38.PMC5343382 10.1186/s12876-017-0583-z
440. Cotton PB, Eisen G, Romagnuolo J, Vargo J, Baron T, Tarnasky P, et al. Grading the complexity of endoscopic procedures: results of an ASGE working party. Gastrointest Endosc. 2011;73(5):868-7410.1016/j.gie.2010.12.036
441. Johnson G, Webster G, Boškoski I, Campos S, Gölder SK, Schlag C, et al. Curriculum for ERCP and endoscopic ultrasound training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2021;53(10):1071-8710.1055/a-1537-8999
442. Sahar N, La Selva D, Gluck M, Gan SI, Irani S, Larsen M, et al. The ASGE grading system for ERCP can predict success and complication rates in a tertiary referral hospital. Surg Endosc. 2019;33(2):448-5310.1007/s00464-018-6317-7