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Short Report

Introduction of Minimally Invasive transCervical oEsophagectomy (MICE) according to the IDEAL framework

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Introduction

The introduction of a novel complex surgical technique is a challenging process, and can be associated with a long learning curve and learning-associated morbidity[1]. During the widespread implementation of transanal total mesorectal excision, the procedure was found to be associated with increased anastomotic leak and local recurrence rates[2]. The LEOPARD-2 trial[3] showed more complication-related deaths after laparoscopic pancreatoduodenectomy.

A succinct and stepwise approach, and systematic assessment of safety and feasibility, along with a rigorous evaluation process from different perspectives, will help limit learning-associated morbidity and prevent unjustified suspension of a potentially beneficial innovative surgical technique. Unfortunately, practical guidelines for the introduction of new surgical procedures, or good examples of the introduction process itself, are lacking.

The aim of this study was to introduce Minimally Invasive transCervical oEsophagectomy (MICE) in a new healthcare setting in a safe way, and to assess how the IDEAL framework may help with this. The present article describes this process from idea to the first-in-human MICE procedures, offering widely applicable steps for other surgical innovators across the world.

MICE procedure

Oesophagectomy with two-field lymphadenectomy is used for the curative treatment of oesophageal cancer[4]. Despite the wide adoption of minimally invasive oesophagectomy, postoperative complications including pneumonia and anastomotic leakage still occur in 20–35 per cent of patients, and have a major impact on hospital and ICU stay, quality of life, and survival[5–7].

MICE is an innovative surgical technique for the treatment of oesophageal cancer. MICE was developed in Japan in 2015, and combines laparoscopic transhiatal and single-port transcervical mediastinal dissection (*Fig. 1*)[8–10]. The technique aims to reduce intrathoracic infectious complications by avoiding transthoracic access without compromising oncological radicality. Preservation of pleural integrity may also limit the sequelae of an anastomotic leak. As a complete upper-to-middle mediastinal nodal dissection and cervical anastomosis is done, an important drawback of MICE might be the increased risk of recurrent laryngeal nerve palsy.

Preclinical stage

The IDEAL framework describes the stages of surgical innovation: Idea, Development, Exploration, Assessment, and Long-term follow-up. In 2019, a Pre-IDEAL stage was added describing preclinical studies (stage 0)[11–13]. A five-step approach (observation, preparation, training, involvement, and evaluation) was developed, and this made the IDEAL framework applicable as a practical guideline before the first-in-human stage (*Fig. 2*); a detailed description is provided in *Appendix S1*.

The observation step (step 1) comprised surgical video analysis and site visits to H. Fujiwara from Kyoto, the founder of the MICE procedure and proctor during the project[8–10].

Preparation (step 2) included a literature search and synthesis of the evidence, and the development of a surgical protocol. Small Japanese (60 patients) and Chinese (80 patients) cohort studies showed MICE to be safe and feasible in terms of duration of operation, blood loss, lymph node yield, pulmonary complications, anastomotic leak rate, and postoperative mortality. Temporary recurrent laryngeal nerve palsy occurred in 19.6 per cent of patients (*Table S1*)[14,15]. Asian studies included mainly patients with squamous cell carcinoma, as opposed to Western patients who are more frequently diagnosed with adenocarcinoma. This is clinically relevant as patient characteristics, co-morbidities, and neoadjuvant treatment differ, which limits the external validity of the published studies[16].

During step 3 (training), MICE was performed on six fresh-frozen human cadavers, supervised by H. Fujiwara and A. Shiozaki, who participated online via a video connection. Cadaver training is

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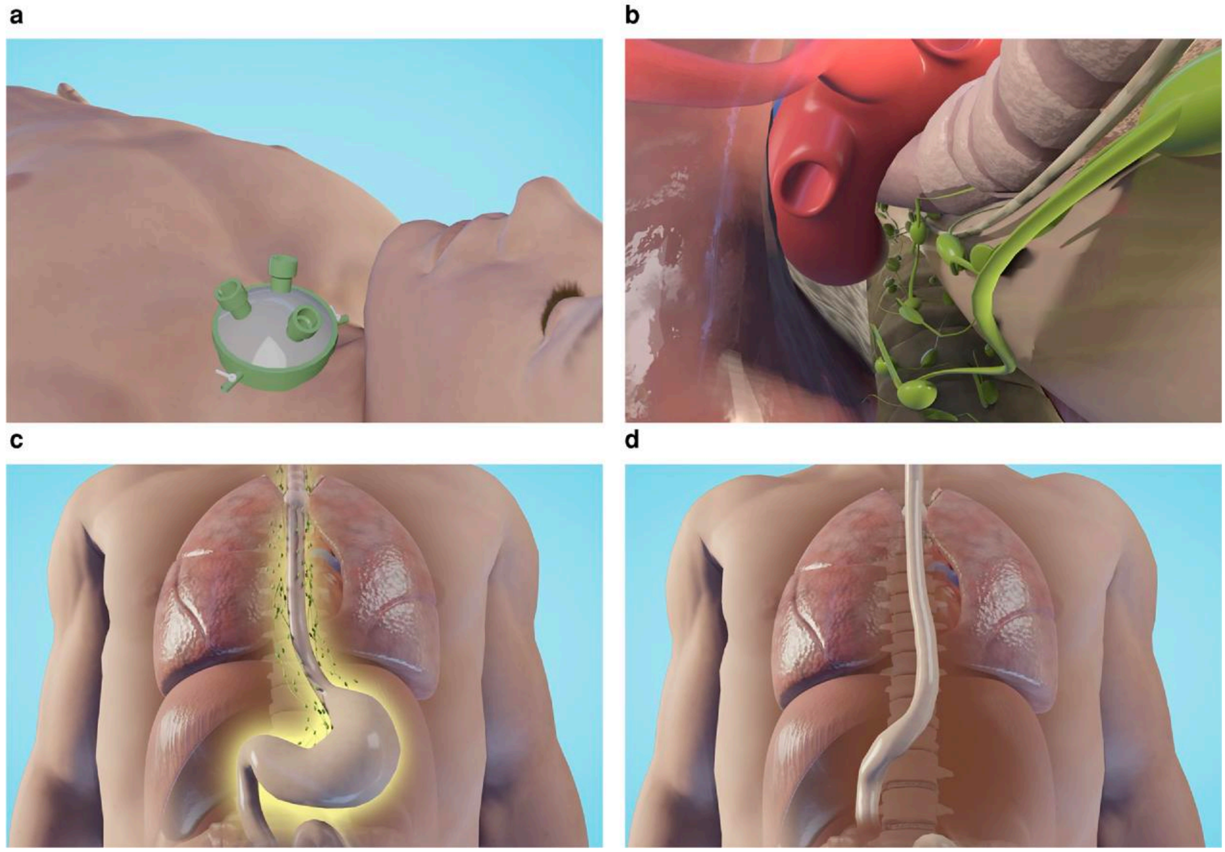

Fig. 1 Minimally Invasive transCervical oEsophagectomy concept
a cervical port placement, **b** transcervical mediastinal dissection, **c** 2-field lymph node dissection, and **d** gastric conduit reconstruction

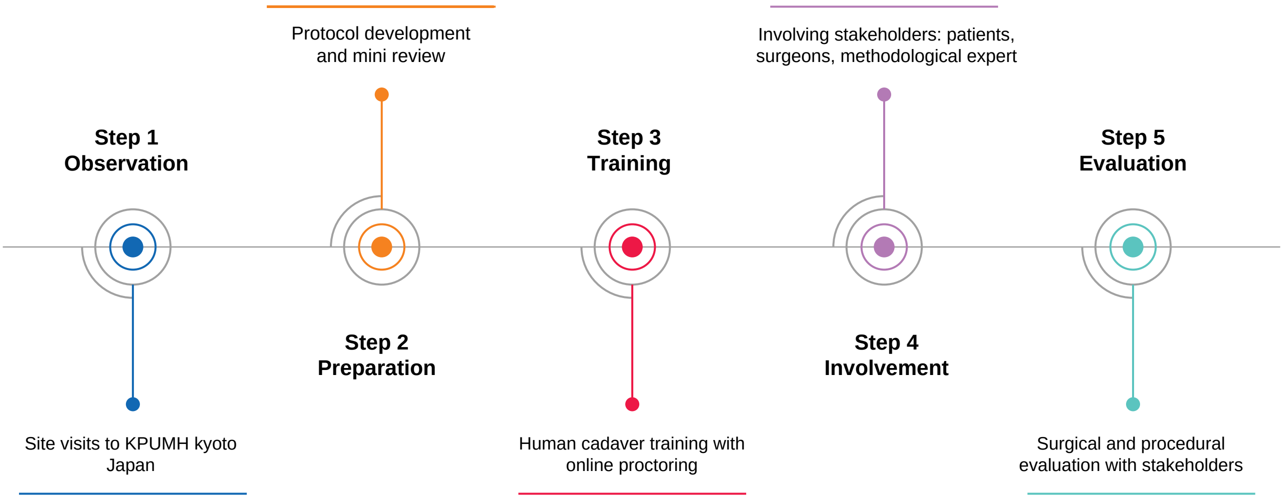

Fig. 2 Five clinically relevant steps during IDEAL stage 0
KPUMH, Kyoto Prefectural University of Medicine Hospital.

thought to be the current standard in training for new surgical techniques[17,18]. A detailed step-by-step surgical workflow was documented before the start of training. The proctors evaluated surgical technique during the cadaver training sessions, and provided feedback before the first-in-human procedure was undertaken. The team did not experience major limitations in the learning process as a result of the virtual set-up.

The following stakeholders were involved (step 4): Dutch patients with oesophageal cancer, representatives of the Dutch upper gastrointestinal patient association, both Japanese expert surgeons, the operating room team of Radboud University Medical Centre, representatives of the Dutch upper gastrointestinal society (oesophageal surgeons and gastroenterologists), and a methodological expert.

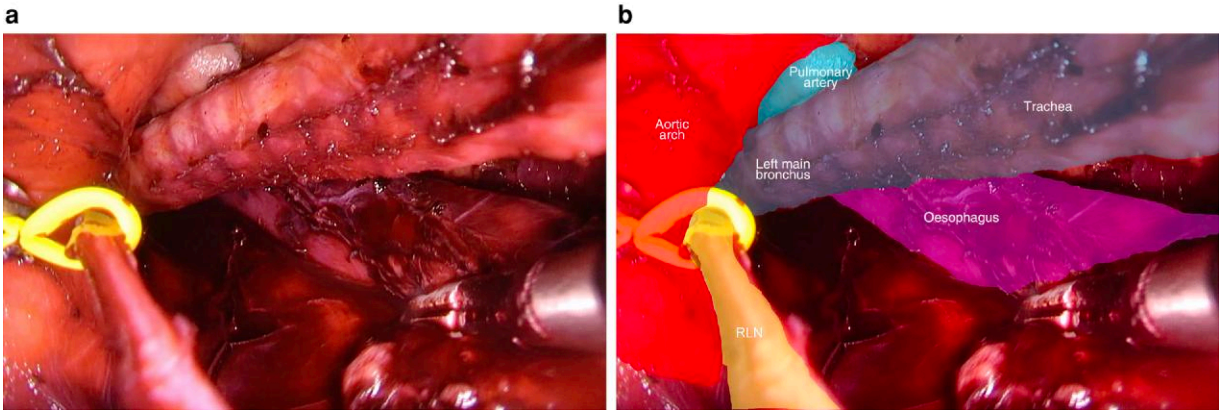

Fig. 3 Surgical view during transcervical mediastinal dissection

a Surgical view during transcervical mediastinal dissection and **b** Same surgical view with anatomical overlays. RLN, recurrent laryngeal nerve.

Prospective risk evaluations (step 5) were conducted, and patient selection and stopping rules were defined with all stakeholders (*Table S2*).

First-in-human study

Three MICE procedures were performed in patients with stage III oesophageal cancer after neoadjuvant chemoradiotherapy, and these were supervised virtually by the Japanese proctors. Details of the operative technique are available in the *supplementary material*, and *Fig. 3* shows a transcervical mediastinal surgical view. Indications for the transcervical approach were: tumours in the upper-to-middle part of the oesophagus, and/or suspected lymph node metastases in the upper mediastinum, and/or squamous cell carcinoma. Conversion to transthoracic minimally invasive oesophagectomy was undertaken in one patient, because of inadequate exposure owing to obesity (BMI 37 kg/m^2). Complications comprised one instance of temporary recurrent laryngeal nerve paresis, and one postoperative haemothorax which was treated by percutaneous drainage. No anastomotic leakage or pneumonia was seen in these three patients. All resections were R0 with a median lymph node yield of 19 (range 19–53). The duration of hospital stay was 8 days for all three patients.

Discussion

The IDEAL framework was used during the introduction of MICE in another healthcare setting to acknowledge the potential additional risks for the first patients to receive this treatment[11–13]. A five-step approach to the preclinical stage was proposed to allow safe progression to the first-in-human stage, with a broad basis of support from clinicians and patients. This process may serve as an example of the safe introduction of other surgical innovations into clinical practice, making the IDEAL framework more applicable as a practical guideline.

The selection of patients who will benefit most from MICE in Western countries is still unclear. Indications for the first three patients in the present study were tumours located in the proximal intrathoracic oesophagus or upper mediastinal lymph node metastases. This group represents approximately 25 per cent of the Dutch oesophageal cancer population. Other indications might be patients who are unfit for transthoracic surgery, such as those with impaired pulmonary function, occupational chest diseases or a history of thoracic surgery. In contrast, when MICE results in fewer pulmonary complications and less severe anastomotic leakage, patients with distal adenocarcinomas might also benefit from this approach[19]. Data from patients in the Western population should elucidate the possible trade-off between pulmonary complications and (temporary) recurrent laryngeal nerve palsy.

After completion of the first two stages of the IDEAL framework, IDEAL stage 2A (development) is under way. This stage is designed to collect data prospectively on the single-centre cohort in Radboud University Medical Centre, optimize the surgical technique, and analyse its outcomes. The establishment of an international community, standardization of the surgical technique of MICE, providing collaborative research on its efficacy, and developing a structured training programme is a prerequisite for safe and successful implementation[20]. Thereafter, the selection of a few high-volume expert centres, development of a rigorous training programme, and the creation of a tool for assessment of competency, might help to mitigate learning-associated morbidity while progressing towards IDEAL stage 2B. Then, a comparative trial of MICE *versus* the standard can be designed to assess the added value of MICE in patients with oesophageal cancer in IDEAL stage 3.

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Author contributions

Bastiaan Klarenbeek (Conceptualization, Methodology, Writing—original draft), Hitoshi Fujiwara (Methodology, Writing—review & editing), Mirre Scholte (Writing—review & editing), Maroeska Rovers (Methodology, Writing—review & editing), Atsushi Shiozaki (Methodology, Writing—review & editing), and Camiel Rosman (Conceptualization, Methodology, Writing—review & editing)

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

Data can be made available upon reasonable request to the corresponding author.

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