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Title Treatment of superficial oesophageal cancer by endoscopic submucosal dissection (ESD)

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Aim

The aim of this report is to assess the efficacy and safety of the endoscopic submucosal dissection (ESD) for the treatment of superficial oesophageal cancer presenting a low risk of node involvement, by comparison to surgery (oesophagectomy) and mucosectomy (or endoscopic mucosal resection, EMR), in order to conclude on the appropriateness of its public funding.

Results

Seventeen publications were analysed to assess the efficacy and safety of ESD compared to surgery and EMR, including one health technology assessment report, five systematic literature reviews with meta-analyses and ten studies published between 2012 and 2018; only one randomised controlled study has been published (in 2017).

The analysis of the literature showed that the available studies, along with those included in the meta-analyses, were mainly retrospective and/or non-comparative, with high risk of bias and having included heterogeneous populations. Moreover, most of the included studies were Asian, with potentially different patient (or lesion) characteristics, management regimens and team experience; the extrapolation of these Asian study results to French practices may not be relevant.

The (very limited) fiver-year overall survival data (primary endpoint) would appear to indicate that there is no significant difference between ESD and oesophagectomy. No publications comparing the overall survival of patients treated by ESD and EMR were identified. The assessment of secondary endpoints would appear to show that the risk of recurrence is lower with ESD than with EMR when the superficial squamous cell carcinoma lesions exceed 20 mm in diameter; there were no available data comparing post-ESD and post-oesophagectomy recurrence rates, whatever the histological type of the superficial oesophageal cancer. In terms of technical efficacy, the en bloc, complete and curative resection rates would appear to be higher with ESD than with EMR for superficial squamous cell carcinoma type lesions. No precise conclusions can be drawn from the results of the quality of life studies. Nevertheless, these results should be interpreted with regard to the aforementioned methodological limitations.

The data on technique-related mortality (primary endpoint), along with procedure-related complications (the most frequent of which were perforation, stenosis and bleeding or haemorrhage) do not allow any precise formal conclusions to be drawn. The data were reported in a descriptive manner, they were derived from low level of evidence studies, frequently including a limited number of patients (for rare expected events), with a frequently relatively short patient follow-up period. The severity of complications was rarely specified, or was reported in an heterogeneous manner, thus precluding any comparisons. An underestimation of complication frequency cannot, therefore, be excluded.

Considering the low level of evidence provided by available literature data, no precise and formal conclusions concerning the superiority or non-inferiority of ESD compared to surgery or EMR can be drawn.

It was pointed out by the stakeholders, however, that in the context of the treatment of an as yet superficial cancer with low risk of node involvement, one of the main advantages of ESD over surgery is organ preservation, thus avoiding functional sequelae associated with surgical excision. Compared to EMR, ESD allows en bloc lesion resection, thus enabling precise anatomopathological analysis of the resected tissues, which is a key phase in patient management. Moreover, ESD provides access to oncological resection treatment in patients for whom surgery is contraindicated. Concerning complications occurring during the procedure, the stakeholders have indicated that, in most cases, these could be treated endoscopically. The duration of hospitalisation would seem to be shorter than for surgery. It was also pointed out that continued monitoring is justified, both after ESD and oesophagectomy, due to the risk of local recurrences and metachronous lesions.

The optimum conditions for performing ESD have been clearly defined, partly in the literature and mainly by the stakeholders involved in this assessment. All patient management-related decisions should be made in a multidisciplinary review meeting. Should operators use ESD to treat a superficial oesophageal cancer deemed to present a low risk of node involvement, the procedure should, according to stakeholder recommendations, be performed under defined conditions, by a trained and

experienced operator in a “reference centre”, or “expert centre”, as it is considered to be a complex technique.

Conclusions

The available literature data thus do not allow any precise and formal conclusions to be drawn concerning the superiority or non-inferiority of ESD compared to surgery or EMR. One of the major advantages of ESD over surgery, however, which was underlined by the stakeholders, is organ preservation, thus avoiding the functional sequelae associated with surgical excision, particularly for a cancer still at the superficial stage and presenting a low risk of node involvement. Compared to EMR, the other endoscopic alternative, ESD allows en bloc lesion resection, thus enabling precise anatomopathological analysis of the resected tissues, which is a key phase in patient management.

Considering all of these elements, HAS considers that ESD may represent a treatment alternative for superficial oesophageal cancer considered to present a low risk of node involvement, subject to the procedure being supervised, as defined in article L.1151-1 of the public health code, with the following recommendations:

- structure: reference centre or expert centre;
- technical platform: level 3 endoscopy centre;
- operator qualification: initial and advanced training required (hepato-gastroenterologist or visceral surgeon, qualified for interventional digestive endoscopy), along with ESD-specific training;
- team composition: a qualified operator, along with a team of anaesthetist and nurse(s) with interventional endoscopy training;
- implementation of a common procedure between the structure and the centre conducting the anatomopathological examination, to ensure that the excised tissue is immediately conditioned and transported under the requisite conditions to ensure high-quality analysis of the resected tissue;
- mandatory implementation of a register for exhaustive recording of ESD-related safety and long-term efficacy data and to ensure that a multidisciplinary review meeting is held, including at the least an interventional digestive endoscopist-gastroenterologist, a digestive surgeon, an anatomopathologist, along with an anaesthetist and resuscitation specialist.

HAS recommends that the choice of treatment regimen be based on a joint medical decision shared by the health care professionals and the patient. This decision must be based on clear and candid information of patients concerning all available techniques, taking into consideration any uncertainties with respect to the added value of the submucosal dissection procedure, along with the follow-up data (particularly long-term) of treated patients.

Moreover, HAS recommends that the ESD safety data, derived from the mandatory register, be reassessed in three years’ time.

HAS recommends conducting a prospective comparative study with long-term patient follow-up and reassessment of the efficacy and safety of ESD at five years, based on the results of this study.

Methods

The assessment method used in this report is based on the critical analysis of the data identified in the scientific literature and the recording of the justified opinion of healthcare professionals, as well as that of a patients' association, in their capacity as stakeholders. A bibliographic search was performed between January 2007 and April 2018, followed by monitoring up to September 2018. The stakeholders were consulted in October 2018.

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