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Endoscopic mucosal resection and endoscopic submucosal dissection for colorectal lesions: A systematic review

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ABSTRACT

Aim: To assess the efficacy and safety of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) for the treatment of colorectal lesions.
Methods: A literature search was conducted from January 2000 to May 2015. The main outcomes were: recurrence after "*en bloc*" and "*piecemeal*" resection; procedure related adverse events; the EMR endoscopic success rate and the completely eradicated resection rate (R0) after ESD.
Results: A total of 66 studies were included in the analysis. The total number of lesions was 17950 (EMR: 11.873; ESD: 6077). Recurrence rate was higher in the EMR than ESD group (765/7303l vs. 50/3910 OR 8.19, 95% CI 6.2–10.9 $p < 0.0001$). EMR-*en bloc* resection was achieved in 6793/10803 lesions (62.8%) while ESD-*en bloc* resection was obtained in 5500/6077 lesions (90.5%) (OR 0.18, $p < 0.0001$, 95% CI 0.16–0.2). Perforation occurred more frequently in ESD than in EMR group ($p < 0.0001$, OR 0.19, 95% CI 0.15–0.24).
Conclusions: Endoscopic resection of large colorectal lesions is safe and effective. Compared with EMR, ESD results in higher "*en bloc*" resection rate and lower local recurrence rate, however ESD has high procedure-related complication rates.

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1. Introduction

Colorectal cancer (CRC) is one of the most common malignancies diagnosed in Western countries, with a rapidly increasing incidence in Asia-Pacific region. CRC screening resulted in an increased diagnosis of a large number of colonic polyps (Jemal et al., 2010; Young and Womeldorph, 2013).

Endoscopic removal of adenomatous polyps reduces the incidence of CRC by 76%–90% (Winawer et al., 1993).

Although the majority of colorectal polyps are less than 10 mm in size and can be routinely removed endoscopically, 0.8%–5% of patients present polyps or non-polypoid lesions (e.g. laterally spreading tumors—LSTs) greater than 20 mm (Iishi et al., 2000; Rembacken et al., 2000).

Invasive cancers may arise more often in these large lesions (Stryker et al., 1987).

Large polyps, even the ones with superficially invasive cancers, can be cured by endoscopic resection as the risk of lymph-node metastasis is lower than 1% when complete removal of lesions with negative microscopic margins (R0-resection) is achieved (Messmann, 2014).

Histological criteria that required to assess a low-risk of lymph-node metastasis are lesions with a submucosal invasion less than 1000 μm, in the absence of lympho-vascular invasion, poor differentiation, tumor budding, and tumor free margin ≥1 mm (Tanaka et al., 2015).

However, the removal of these lesions may be challenging and incomplete resection resulting in early recurrence may occur. In these patients, the scarring complicates further attempts of endotherapy (Hori et al., 2014).

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have broadened the therapeutic possibilities of interventional endoscopy, reducing the number of patients who would have been referred to surgical resection (Soetikno and Gotoda, 2009; Kaltenbach et al., 2008).

If compared with surgery, endoscopic resection provides the advantage to be less invasive, requiring short hospital stay and rapid discharge, with lower costs (Repici et al., 2009; Longcroft-Wheaton et al., 2013; Swan et al., 2009).

EMR has been extensively used throughout the gastrointestinal tract to remove early neoplastic lesions; it is widely accepted for the treatment of colon adenomas and superficial colorectal tumors (Swan et al., 2009; Bergmann and Beger, 2003; Su et al., 2005; Bories et al., 2006; Katsinelos et al., 2006; Arebi et al., 2007; Hurlstone et al., 2008; Urban et al., 2008; Mahadeva and Rembacken, 2009; Luigiano et al., 2009; Huang et al., 2009; Lim et al., 2010; Ferrara et al., 2010; Conio et al., 2010a; Saito et al., 2010a; Toyonaga et al., 2010; Hochdörffer et al., 2010; Moss et al., 2011; Kao et al., 2011; Tajika et al., 2011; Santos et al., 2011; Mannath et al., 2011; Kim et al., 2012; Lee et al., 2012; Kobayashi et al., 2012; Fasoulas et al., 2012; Buchner et al., 2012; Binmoeller et al., 2012; Terasaki et al., 2012; Carvalho et al., 2013; Kim et al., 2013; Masci et al., 2013; Dior et al., 2013; Cipolletta et al., 2014; Maguire and Shellito, 2014; Gómez et al., 2014; Grgov et al., 2014; Belle et al., 2014; Knabe et al., 2014; Wang et al., 2014a; Kim et al., 2014; Kashani et al., 2015; Hong et al., 2015; Curcio et al., 2015; Oka et al., 2015; Voudoukis et al., 2015; Binmoeller et al., 2015).

In these cases "*en bloc*" resection is mandatory, allowing a histological assessment of lateral tumor margins; the rates of "*en bloc*" resection have been determined to be as high as 66.6–80% in EMR, when the tumor size was <20 mm (Nakajima et al., 2013).

Unfortunately large lesions require "*piecemeal*" resection, increasing the risk of recurrence (Fujiya et al., 2015a). Recent data reported an incomplete resection rate significantly higher for "*piecemeal*" compared to "*en-bloc*" resection (18.9 vs. 12.6%, p = 0.01) (Cipolletta et al., 2014).

Lesions such as LSTs should be removed "*en-bloc*", giving the higher frequency of submucosal invasion (Uraoka et al., 2006; Oka et al., 2009).

In particular, the risk of incomplete resection is high when EMR is used to resect nodular mixed type LSTs (LST-G, mixed type) ≥30 mm and LST-non granular type (LST-NG) ≥20 mm in size, having a risk of submucosal invasion from 11.1% to 19% according to lesions size (Imai et al., 2014; Fujishiro et al., 2007; Saito et al., 2013; Matsuda et al., 2010; Yamamoto et al., 2002). Only uniform LST-G, would be suitable for piecemeal resections as the risk of submucosal invasion is very low (1.8%) (Imai et al., 2014).

To overcome EMR limitation, ESD has been proposed for lesions that need to be resected "*en-bloc*" in order to allow an adequate histologic assessment (Tanaka et al., 2015). Moreover, lesions that would be very difficult to resect by conventional EMR from the technical viewpoint are also considered as an indication for ESD, including the lesions showing poor- or non-lifting after submucosal injection, local recurrent lesions following previous treatment, and relatively large protruded type lesions (Saito et al., 2010a; Toyonaga et al., 2010; Tajika et al., 2011; Lee et al., 2012; Kobayashi et al., 2012; Terasaki et al., 2012; Kim et al., 2013; Oka et al., 2015; Fujishiro et al., 2007; Saito et al., 2013; Matsuda et al., 2010; Yamamoto et al., 2002; Saito et al., 2001, 2007; Tanaka et al., 2007; Tamegai et al., 2007; Hurlstone et al., 2007; Isomoto et al., 2009; Niimi et al., 2010; Saito et al., 2010b; Takeuchi et al., 2010; Uraoka et al., 2011; Probst et al., 2012; Iacopini et al., 2012; Lee et al., 2013; Xu et al., 2013; Repici et al., 2013; Rahmi et al., 2014; Białek et al., 2014; Agapov and Dvoinikova, 2014; Spychalski and Dziki, 2015).

Recently, the guidelines of the European Society of Gastrointestinal Endoscopy (ESGE) recommended endoscopic "*en bloc*" resection by ESD for "removal of colonic and rectal lesions with high suspicion of limited submucosal invasion that is based on two main criteria of depressed morphology and irregular or non granular surface pattern, particularly if the lesions are larger than 20 mm; or for colorectal lesions that otherwise cannot be optimally and radically removed by snare-based techniques" (Pimentel-Nunes et al., 2015).

The aim of the present systematic review is to assess efficacy and safety of EMR and ESD in the management of large colorectal lesions.

2. Methods

The reporting of this systematic review follows the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati et al., 2009).

2.1. Study selection

A literature search was conducted using Pubmed (MEDLINE), Embase, and the Cochrane Central Register Controlled Trials, from January 2000 to May 2015, using the terms:

- (endoscopic mucosal resection AND/OR EMR) AND (colorectal lesion OR polyp OR laterally spreading tumor OR LST)
- (endoscopic submucosal dissection AND/OR ESD) AND (colorectal lesion OR polyp OR laterally spreading tumor OR LST)

Enter terms for research on the Cochrane Central Register Controlled Trials were "endoscopic resection AND colon".

The search was conducted on all English language published articles and including exclusively human studies. The complete manuscript of all relevant studies was retrieved and reference lists were searched to identify any additional relevant papers. When