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Title

Multi-disciplinary decision-making strategies may reduce the need for **secondary** surgery in complex colonic polyps - a systematic review and pooled analysis

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Abstract

Aim

The recognition of complex colonic polyps is increasing. Management varies considerably and the impact of this on clinical outcomes is unclear. The aim of this systematic review was to assess the impact of group decision-making strategies and defined selection criteria on the treatment outcomes of complex colonic polyps.

Method

A systematic literature review identified studies reporting complex polyp treatment outcomes and describing their decision-making strategies. Databases searched included PubMed, Web of Science, CINAHL and Scopus. Articles were identified by two blinded reviewers using defined inclusion criteria. The review protocol was registered on PROSPERO and performed in line with PRISMA guidelines.

Results

There were 303 identified articles describing treatment outcomes of complex colonic polyps. Only 9 of these fully described the decision-making strategy and met the inclusion criteria. Adverse events ranged from 1.3% to 10% across the studies. Unsuspected malignancy and secondary surgery rates ranged from 2.4% to 15.4% and 3.3% to 43.9% respectively. Grouping of articles into a hierarchy of decision-making strategies demonstrated a sequential reduction in secondary surgery rates with improving strategies. There were no differences in comparisons of adverse event or unsuspected malignancy rates.

Conclusion

There is limited description of decision-making strategies and variability in reporting of studies describing complex polyp treatment outcomes. The use of multi-disciplinary decision-making and defined selection criteria may reduce the need for **secondary surgical intervention** in complex colonic polyps, but further evidence is required to draw definite conclusions.

Keywords

Complex colonic polyps, decision-making, outcomes

What does the paper add to the literature?

Decision-making in multi-disciplinary teams has been recommended to improve treatment outcomes of complex polyps but with little supporting evidence. This review identifies limited reporting of decision-making strategies in the literature. The available evidence suggests better strategies may reduce the need of **secondary surgical intervention** for complex polyps, but further work is needed.

Introduction

Colorectal cancer accounts for 11% of cancer diagnoses annually in the UK (1) with 54% estimated as being preventable (2). Early detection improves outcomes and removal of pre-malignant polyps also reduces incidence of subsequent colorectal cancer as well as mortality associated with it (3).

Bowel cancer screening aims to detect asymptomatic cancer, but many polyps are also identified. Most are easily removable, but **some** are challenging and detection of complex polyps is increasing (4). There is no internationally standardised definition, but they are generally accepted **as those** larger than 20mm or in a location making endoscopic removal difficult (5, 6). The British Society of Gastroenterology (BSG) guidelines also include **polyps** with a site morphology size access (SMSA) level of 4 or with increased risk of malignancy, incomplete resection or adverse events (7). Early cancer is found in 10-15% (7) so treatment should be individualised and balance complete polyp removal against the risks of intervention. Management strategies vary considerably (8, 9) and the reasons for this are unclear.

Guidelines recommend endoscopic therapy when cancer is not suspected (10) which has **fewer** adverse events and shorter hospital stays compared to surgery (11, 12). Combined endoscopic and laparoscopic procedures can also avoid colonic resection in selected cases (13, 14). Surgery for benign polyps may be indicated for some but the proportion having bowel resections is considered a key performance indicator (7, 15). In those found to have malignancy **on final histology**, survival and disease recurrence does not seem adversely affected by an initial endoscopic attempt (16).

A multi-disciplinary decision-making process involves defined selection criteria for treatment applied by a group of **individuals** with complementary expertise. The impact of **such** strategies on complex polyp outcomes is unclear (17) but utility has been demonstrated in other settings (18, 19). **The outcome of good decision-making should be providing the most appropriate management for a patient and their polyp at first attempt.** BSG guidelines recommend the use of multidisciplinary teams (MDT) for complex polyp management but based on very little evidence (7).

Given the variation in practice for complex polyp management, the effect of group decision-making and selection criteria merits investigation. The primary aim of this review was to assess the impact of these clinical decision-making strategies on the treatment outcomes of complex colonic polyps.

Methods

A systematic literature review was performed to identify studies reporting treatment outcomes of complex colorectal polyps and describing decision-making strategies for management.

Definitions

Complex colonic polyp

The definition of complex polyps included those described as difficult, advanced, large, significant, refractory or endoscopically unresectable in literature. Non-pedunculated polyps larger than 20mm (5, 6), those with an SMSA level of 4 (7), with an increased risk of malignancy, incomplete resection or adverse events (7) or in a difficult location (5, 6) were also included.

Defined and undefined selection criteria

Defined selection criteria were articles using specified parameters such as size, location or morphology justifying their treatment choice. Undefined selection criteria were where treatment was chosen on the opinion of a clinician without elaboration of the factors considered.

Adverse event rate

Adverse events were described using the Clavien-Dindo (CD) classification system (20). Adverse events of CD 2 or higher were used to calculate the adverse event rate. As CD 1 events do not require intervention, they were not included. This was described per number of patients in the study.

Suspected and unsuspected malignancy rates

Suspected malignancies were lesions identified as such by endoscopic assessment or biopsy before or at the primary procedure. Unsuspected malignancies were those recognised on final histology. If there was ambiguity, the Vienna classification was applied (21). Unsuspected malignancy rate was the primary outcome as further treatment would need to be considered and selected early cancers may be appropriately treated with endoscopy. This was described per number of lesions in the study

Primary and secondary surgery rate

Primary surgery rate was those referred directly without attempt at endoscopic therapy. Secondary surgery were patients having a colonic resection for any indication thereafter. This was described per number of patients in the study.

Residual and recurrent disease

Residual disease was that occurring at the resection site within 3 months of treatment (10). Recurrent disease was defined as occurring after this. This was described per number of patients followed-up in the study.

Literature search and search terms

Relevant full text articles were systematically identified from the literature based on the inclusion and exclusion criteria. The study protocol was registered in PROSPERO (22) and performed in line with the PRISMA guidelines (23).

Databases searched included PubMed, Web of Science, CINAHL and Scopus. Updates to identify new articles until the start of analysis in November 2020 were used. No individual journals or country of publication were excluded. All articles were initially considered regardless of **publication** year or language.

The search terms were developed with expertise in complex polyps and utilised strategies from published guidelines (7). Terms included 'colonic polyps', 'complex', 'difficult', 'advanced', 'endoscopically unresectable', 'refractory', 'laterally spreading', 'large', 'polypectomy', 'endoscopic mucosal resection', 'endoscopic submucosal dissection', 'surgery', 'operate', 'laparoscopic', 'combined procedure', 'hybrid procedure' and 'laparoscopic facilitated'. Search terms were broad considering the variability in complex polyp terminology. The full strategy **is shown** in supplementary material 1.

Inclusion criteria

Articles reporting colonic polyp **management** were assessed against our complex polyp definition. Articles meeting this were then reviewed against the decision-making inclusion criteria which included the responsible clinician(s) making the decision and how the decision was reached. Finally, studies had to describe primary outcomes of adverse events, **malignancies**, or surgery. Secondary outcomes including length of stay, residual or recurrent disease, functional outcomes and cost analysis were assessed if described.

Exclusion criteria

Studies reporting on malignant polyps, rectal polyps, paediatric patients, polyposis syndromes or inflammatory bowel disease were excluded due to the separate considerations required in these circumstances.

Reports on novel techniques or devices were not considered as decision-making and patient selection may be biased. Posters, presentations, case reports or editorials were excluded. Despite considering all articles, some were unavailable despite reasonable efforts to obtain them or lack of language expertise.

Article identification

Database search results were downloaded into EndNote to identify duplicates. Abstracts were then exported to the Rayyan Systematic Review Web Application (24). Two independent, blinded researchers screened abstracts against our criteria. The researchers resolved conflicts and finalised articles for full text review. Any unresolved conflicts were referred to the senior researcher. Full text articles were assessed by the same blinded reviewers and managed on separate EndNote files. Those meeting the inclusion criteria were selected for data extraction. Review articles and guidelines utilising systematic literature searches were cross referenced to identify additional studies. The abstracts identified were reviewed using the same process.

Data extraction and analysis

Data extraction was performed by the same blinded researchers onto separate, pre-defined spreadsheets. Variations in data extraction were resolved and finalised between the researchers and senior author.

Analysis was performed by one researcher and cross checked by a second using Microsoft Excel and SPSS.

Articles were classified into three groups based on their decision-making strategies.

<i>Group 1</i>	Used defined selection criteria and multi-disciplinary decision-making
<i>Group 2</i>	Used defined selection criteria and individual decision-making
	Or
	Used undefined selection criteria and multi-disciplinary decision making
<i>Group 3</i>	Used undefined selection criteria and individual decision-making

Given the clinical heterogeneity and small number of **case series**, a meta-analysis was **deemed inappropriate**. Statistical heterogeneity of the groups was assessed with chi-squared tests. A pooled analysis of primary outcomes was performed to allow **group comparisons** using chi-squared tests. A P value of <0.01 was accepted as significant.

Assessment of study quality

The methodological quality of studies was assessed by the Specialist Unit for Review Evidence (SURE) questions to assist with the critical appraisal of case series (25) independently by two researchers (supplementary material 2). A narrative description was performed due to the **absence of** evidence supporting scales in assessing study quality (26).

Results

Study selection

A total of **6,211 articles were screened and an** overview is shown in figure 1. There were 303 articles matching our complex polyp definition and describing treatment outcomes. Decision-making strategies were not described in 233 (76.9%), and there were 59 (19.5%) articles only partially describing their strategy. One article only reported mortality as its outcome and was excluded. Another article met the inclusion criteria but was published in 1977. As polyp therapy was very different at this time, a collaborative decision was made to exclude this. This left nine articles in the final analysis (27-35). Categorisation of excluded articles is described in supplementary material 3.

Study characteristics

A summary of the studies is shown in table 1. All were single centre, observational case series. Six studies were retrospective (27, 29-32) and three prospective (28, 33, 35). Patient age ranged from 29 to 99 years. A total of

1,086 lesions in 1,037 patients were included and size ranged from 10mm to 160mm. Four studies described endoscopic treatments in the form of polypectomy, endoscopic mucosal resection or endoscopic submucosal dissection (30, 32-34). Four studies described combined endoscopic and laparoscopic procedures (27, 29, 31, 35) and one study both endoscopic and combined techniques (28).

Decision-making strategies

Table 2 summarises the decision-making strategies used. Group decisions (two or more clinicians) were used by three studies (27, 30, 32) with only one utilising an MDT (27). Six studies based management on the advice of an individual clinician. There were no articles comparing outcomes of groups using different decision-making strategies.

Six studies were categorised as having defined selection criteria (27-32). Polyp factors were the commonest parameter used for decision-making. This included size (n=6), lesion location (n=6), surface changes and morphology (n=3), pre-intervention histology (n=3), evidence of malignancy (n=2), lifting sign (n=2), risk of incomplete resection (n=1) and recurrences (n=1). Two papers considered patient co-morbidities when deciding management. The remaining three studies used undefined selection criteria subject to a clinician's opinion (33-35). **No study described the use of shared decision-making with the patient.**

Primary outcomes

Table 3 shows a summary of the primary outcomes reported by the included studies.

Primary and secondary surgery rates

Three articles reported the number referred for primary colonic resection (28, 33, 34) (table 1) with a wide variation of 9.1% (33), 33.8% (34) and 57.8% (28). **Two of these studies used individual decision-makers and undefined selection with secondary surgery rates of 8.2% (33) and 43.9% (34). The final study described individual decision-maker with defined selection criteria and a secondary surgery rate of 5.3% (28).** Only two included treatment outcomes for those having primary resections (28, 34). **Due to this these patients were excluded, and further statistical analysis was not performed.**

The secondary surgery rate ranged considerably from 3.3% to 43.9%. The commonest indication for colonic resection was an unsuccessful or incomplete endoscopic resection (n=90). Other indications included cancer detected on final histology (n=20), cancer suspected at polyp assessment during procedure (n=19), recurrence (n=5) and perforation (n=3).

Adverse event rates

Adverse event rates across the studies ranged from 1.3 to 10%. The number of CD 1 events reported ranged widely from 2.6% (30) to 51.6% (34) with most being conservatively managed rectal bleeds. There was no mortality in any study. There were two CD 4 adverse events reported by a single study (29). These were an anaesthetic related anaphylaxis and pulmonary embolism in a single patient having a combined procedure.

Unsuspected malignancy rates

Unsuspected malignancies ranged from 2.4% to 15.4% across the articles. A complete overview of is provided in supplementary material 4.

Secondary outcomes

Length of stay was reported in six studies. It was generally short with a range of averages between 0 and 2 days (27-31, 35). Bulut was the only study reporting length of stay for colonic resections separately which ranged from 4 to 12 days (27).

Duration of follow-up ranged from 6 to 50 months with variability in surveillance timings and number receiving follow-up. One study did not state the duration of follow-up (35). Table 4 summarises residual and recurrent disease. Residual disease incidence ranged from 7.8% (30) to 20.4% (32) of the three reporting studies. Eight studies described recurrent disease ranging from 0% (31) to 34% (34). Only one paper reported follow-up endoscopy for all study patients (31).

No study assessed functional, or patient reported outcomes. Two papers performed a cost analysis. Cohan compared costs for endoscopic step-up management against patients having planned colectomy (28) demonstrating a cost saving for the former. Longcroft-Wheaton found a significant cost reduction with endoscopy compared to surgery (33).

Pooled analysis and comparison of decision-making groups

Articles were classified into three groups as described previously. There was no significant heterogeneity in adverse event rates (group 1 $p=0.67$, group 2 $p=0.94$, group 3 $p=0.08$) as calculated by chi-squared tests. The heterogeneity in unsuspected malignancies (group 1 $p=0.00$, group 2 $p=0.98$, group 3 $p=0.30$) and secondary surgery (group 1 $p=0.00$, group 2 $p=0.05$, group 3 $p=0.00$) varied within the groups.

The pooled adverse event and unsuspected malignancy rate across the three groups were similar ranging from 3.8% to 9.2% and 3.1% to 6.1% respectively (table 5). There were sequential decreases in secondary surgery with improving decision-making strategies. Pooled secondary surgery rate was 6.0% in those articles categorised into group 1 compared to 23.3% in group 3.

The reduction in secondary surgical intervention with improved decision-making strategies was significant (table 6). There was no difference in comparisons between groups regarding unsuspected malignancy. Adverse events were significantly lower in group 3 as compared to group 2 but not in any other comparison in this category.

Assessment of paper quality

The studies were assessed by the SURE questions and classified into whether the article met the criteria, did not meet the criteria or was unclear. Most criteria were achieved by the articles and were deemed to be of reasonable to good quality by the researchers.

Criteria for the study aims and design, setting and dates, selection criteria, enrolment, participants characteristics, outcome measures and results were met by all articles. Two studies did not meet the criteria regarding participant flow due to inadequate follow-up (27, 35). The quality of statistical methods was not well described in most studies excluding Emmanuel and Kao (30, 32). This was due to either incomplete statistics or absence of discussion regarding missing data or confounding factors. Most articles identified the limitations of their research, but two studies did not (34, 35). Only one paper declared a conflict of interest (28). The remaining articles either had no conflicts (27, 29-33) or it was unclear (34, 35).

Discussion

MDT strategies involving group decision-making and defined selection criteria **for complex colonic polyps may improve patient** outcomes by **avoiding the need for secondary procedures**. This is the first evidence attempting to assess the impact of such strategies. This review also demonstrates the lack of decision-making and **variation in outcome reporting** concerning **complex polyp** management.

Decision-making strategies may have a higher impact in diseases with wider variation in management (36, 37). This review aimed to identify evidence supporting these approaches to complex polyps **but there were** challenges given the review's **novel design** and lack of **preceding** literature. Group decisions utilising selection criteria are key features of an MDT and were therefore the chosen parameters. Of the many articles identified, only a small number were suitable for inclusion and only one used an MDT (27). They were mostly small, case series with a variety of procedures described. This was recognised, but as they were all based on first line endoscopic resections and the comparator was decision-making, this was accepted by the study team. **No** studies **compared** outcomes of groups where different decision-making strategies were applied which is a significant limiting factor. Our initial aim was to **report primary** surgery rates which is currently thought to be around 12.8% (9). Given only three studies reported it, this was not suitable for more than a descriptive assessment. Insight to surgically **treated** complex polyps is important as complication and mortality rates are 24% and 0.7% respectively (38) with readmission (7.8%) and stoma formation (2.2%) also a risk (39).

Guidance on performing **systematic** reviews of observational studies **is** conflicting (40) and created challenges **regarding the analysis** and **reporting of findings**. A pooled analysis to allow comparison **of** groups with assessment of heterogeneity was a pragmatic solution but we acknowledge the limitations of this.

The outcome of good decision-making should be providing the most appropriate management for a patient and their polyp at first attempt. This requires a thorough and accurate assessment to allow fully informed and shared decisions to be made. If this process is robust, the need for secondary procedures should be avoided and could be considered a reflection of good decision-making. Grouping of articles into a hierarchy of decision-making demonstrated a sequential reduction in the need of a secondary procedure with improving strategies. The arbitrary assignment of studies to decision-making groups is a surrogate for the true underlying process but was a pragmatic method of assessment. Given the limitations of the review and statistical heterogeneity within some groups, we cannot be certain these are true effects. It does provide the first evidence supporting decision-making in improving outcomes and will hopefully promote generation of further **research**.

The use of strict polyp selection criteria when identifying articles aimed to reduced variability in the study population but differences remained in patient characteristics and selection criteria which affects generalisation and comparability of results. This may explain the wide ranges in the outcomes but may also reflect significant variability in practice as reported previously (8, 9). We advocate standardisation of articles concerning complex polyps. Studies should include the denominator stating those managed with other methods including conservatively or with surgery. We suggest that a full description of the patient and polyp population, decision-making strategies involved and clear classifications of outcomes including surgery, complications, recurrence and adverse events should be reported with an adequate follow-up as a standardised minimum dataset (41). Qualitative assessments of decision-making in patients and clinicians regarding malignant polyps have been reported (42) and is likely these complexities also apply to benign polyps. Patient involvement in decision-making should be encouraged and reported as part of article standardisation.

Despite the limitations of this review, developing evidence in this field is required given the variability in management and increasing detection of complex polyps. Good decision-making practices may benefit patient outcomes. Further evidence is required directly comparing decision-making strategies using standardised reporting. Assessments of centres using an MDT and understanding decision-making on an individual level are also important. In addition to the treatment outcomes, assessment on patient quality of life and experience, functional outcomes and financial impacts also need to be evaluated.

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