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Obstructing colorectal cancer: a population-based review of colonic stenting in Queensland, Australia

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Purpose: Stenting is a useful treatment option for malignant colonic obstruction, but its role remains unclear. This study was designed to establish how stents have been used in Queensland, Australia, and to review outcomes.

Methods: Patients diagnosed with colorectal cancer in Queensland from January 1, 2008, to December 31, 2014, who underwent colonic stent insertion were reviewed. Primary outcomes of 5-year survival, 30-day mortality, and overall length of survival were calculated. The secondary outcomes included patient and tumor factors, and stoma rates.

Results: In total, 319 patients were included, and distant metastases were identified in 183 patients (57.4%). The 30-day mortality rate was 6.6% (n = 21), and the 5-year survival was 11.9% (n = 38). Median survival was 11 months (interquartile range, 4–27 months). A further operation (hazard ratio [HR], 0.19; P < 0.001) and chemotherapy and/or radiotherapy (HR, 0.718; P = 0.046) reduced the risk of 5-year mortality. The presence of distant metastases (HR, 2.052; P < 0.001) and a comorbidity score of 3 or more (HR, 1.572; P = 0.20) increased mortality. Surgery was associated with a reduced risk of mortality even in patients with metastatic disease (HR, 0.14; P < 0.001). Twenty-two patients (6.9%) ended the study period with a stoma.

Conclusion: Colorectal stenting was used in Queensland in several diverse scenarios, in both localized and metastatic disease. Surgery had a survival advantage, even in patients with metastatic disease. There was no survival difference according to whether patients were socioeconomically disadvantaged, diagnosed in a major city or not, or treated at private or public hospitals. Stenting proved a valid treatment option with low stoma rates.

Keywords: Colorectal neoplasms; Intestinal obstruction; Self expandable metallic stents; Colonoscopy

INTRODUCTION

Colorectal cancer (CRC) is the 4th most common cancer and the second highest cause of cancer mortality in Australia [1]. It accounts for about 11% of cancer diagnoses, with an overall incidence in Queensland, of 3,000 to 3,500 cases per annum. It is estimated that between 10% and 20% of patients present with bowel obstruction [2, 3]. Historically, obstructing CRC has been primarily managed with emergency surgery and the Hartmann procedure. However, patients undergoing emergency surgery have higher morbidity and mortality than those undergoing elective operations [4].

As a potential means to address this disparity in outcomes, colonic stenting as a treatment option has been available since the

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development of self-expanding metal stents in the 1990s [5]. A colonic stent is a self-expanding wire-mesh tube that can re-create luminal patency and lead to colonic decompression in patients with a large bowel obstruction. Inserted and deployed endoscopically, colonic stents offer immediate non-operative resolution of colonic obstruction, providing an opportunity for the optimisation of the patient for elective surgery.

Colorectal metal stents present an attractive therapeutic option in the management of obstruction without the immediate requirement of resection. The role of colorectal stenting in the treatment of obstructing CRC, particularly as a bridge to surgery, is unclear. Some studies have suggested that its main use is in palliative management [6], while others have reported better outcomes in patients undergoing stenting procedures as a bridge to surgery [7]. A 2017 guideline update from Cancer Council Australia [8] recommended that stents as a bridge to surgery, in potentially curative CRC, should not be the standard of care in curative intent cases (grade D evidence), but remain a preferred management strategy in the palliative setting. This recommendation is primarily due to the risk of perforation and has resulted in the premature closure of 2 randomized controlled trials [9, 10]. A recently published meta-analysis by Balciscueta et al. [11] shows an increased risk of locoregional recurrence and overall recurrence when stenting malignant large bowel obstructions as a bridge to surgery.

There is also the risk of stent migration and restenosis [12], and delayed perforation is seen when combined with vascular endothelial growth factor inhibition immunotherapy [13]. The use of colorectal stents in obstructing CRC as a bridge to surgery remains an option in high-risk patients with curable CRC or as a palliative measure (consensus statement) [8].

This study interrogated a state-wide population-based registry of all colorectal cancers diagnosed over 7 years and assessed the short and long-term outcomes of colorectal stenting in the management of obstructing CRC in Queensland.

METHODS

Ethics statement

This study was approved by the Human Research and Ethics Committee of the Royal Brisbane and Women's Hospital (No. LNR/2021/QRBW/72957). The requirement for informed consent was waived due to the retrospective nature of the study.

Study design and setting

In Queensland, Australia, reporting of all malignancies to the Queensland Cancer Register (QCR) is mandated by law. These data are managed by the Cancer Alliance Queensland, which links the data from the QCR with over 60 other population-level sources including hospital admissions, treatment, public and private pathology, and mortality data into the Queensland Oncology Repository (QOR). By accessing this combined repository, a complete population-wide analysis of endoscopic stenting of an obstructing colorectal cancer was performed.

The primary objective was to assess patient outcomes following the insertion of a colorectal stent at the time of emergency admission for obstructing CRC. The secondary objectives were to assess the patient and demographic factors associated with colonic stent placement in obstructing CRC; and to calculate stoma rates.

Patients

Patients from the repository were included if they underwent an endoscopic stent procedure and had a diagnosis of CRC of any morphology. There were no exclusion criteria.

Patient demographics (including age, sex, location [metropolitan, remote, rural] and socioeconomic status), as well as comorbidities, cancer details, and survival outcomes were recorded. Socioeconomic status was defined using the 2011 Index of Relative Socioeconomic Disadvantage [14] and patients were categorized into disadvantaged, middle, and affluent groups. Patient comorbidity scores were counted from a list: AIDS, prior myocardial infarction, cancer (other than the primary colorectal cancer), cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, dementia, diabetes, complications from diabetes, hemiplegia or paraplegia, liver disease, peptic ulcer disease, peripheral vascular disease, renal disease, and rheumatoid/connective tissue disease. These comorbidity scores and American Society of Anesthesiologists (ASA) physical status (PS) were dichotomized into comorbidity scores of 0 to 2 (normal or mild disease) and 3 or more (severe disease).

The 30-day mortality rate was calculated based on the number of deaths within 30 days after the placement of a colorectal stent. Five-year survival was calculated, and death was defined as death within 5 years from the date of cancer diagnosis. Length of survival was calculated from the date of diagnosis to the date of death, while for patients still surviving at the study end-date, the length of survival was calculated from the date of diagnosis to December 31, 2019.

Statistical analysis

Baseline characteristics were summarized using descriptive statistics. All categorical data were analyzed using either the Fisher exact test or Pearson chi-square test. Continuous data were analyzed using the Student t-test. Kaplan-Meier curves were used to plot length of survival. Cox regression analysis was used in multivari-

ate analysis. Analysis was undertaken using IBM SPSS ver. 25.0 (IBM Corp). A P-value <0.05 was considered significant.

RESULTS

From an initial dataset of 20,063 patients between January 1, 2008, and December 31, 2014, a total of 319 patients were identified who underwent colonic stent placement for obstructing CRC. The demographic, medical background, and tumor data of these patients are summarized in Table 1. Many data fields were complete or near complete. ASA PS and comorbidity data were missing in 101 and 47 cases, respectively. These parameters are not currently mandated, and physical chart reviews for missing data points was not possible with the resources available.

The 30-day mortality rate was 6.6% (n=21). A correlation was found between surgery within 1 week of stenting and an increased risk of 30-day mortality (P<0.001). The 5-year survival rate was 11.9% (n=38). The mean survival was 21.26 months (95% confidence interval [CI], 18.18–24.34 months; median, 11 months; interquartile range, 4–27 months). Surgery within 1 week of stenting did not affect 5-year survival (P=0.12) or overall survival (P=0.28).

Several factors impacted overall survival, as shown in Table 2. A further operation (hazard ratio [HR], 0.190; P<0.001) and treatment with chemotherapy or radiotherapy or both (HR, 0.718; P=0.046) had a positive impact on survival. Presence of distant metastases (HR, 2.052; P<0.001) and a comorbidity count of 3 or more (HR, 1.572; P=0.020) had a negative impact on survival. Sex, age (under 80 years vs. 80 years or more), socioeconomic status, living in a major city, and hospital type (private vs. public hospital) did not have statistically significant impacts on survival. Likewise, different tumor characteristics showed no significant effects (adenocarcinoma vs. other histological subtypes, or high-grade cancer). Kaplan-Meier analysis suggested improved outcomes in cancers diagnosed after 2010, but this was not shown to be statistically significant in the Cox regression or bivariate analysis (P=0.10).

The mean age for the group was 70.92 years (range, 21–99 years; 95% CI, 69.32–72.51). The mean age was higher in the group that did not proceed to surgery after stenting (73.16 years vs. 66.54 years, P<0.01). The majority of patients were male (n=204, 63.9%).

The socioeconomic status of the patients was described as disadvantaged for 70 (22.0%), middle class for 207 (65.1%), and affluent for 41 (12.9%). A majority of patients (69.3%) were from major cities, while 19.1% came from inner regional areas, 10.0% from outer regional areas, and 1.3% from remote areas. Furthermore, 189 patients (59.2%) were treated in a public hospital.

The ASA PS was recorded for 218 patients, of whom 78.4% had a high ASA PS (ASA PS, III–VI). Data on the comorbidity count were missing in 47 patients, and of the remaining 272, 71 (26.1%) had a comorbidity count of 3 or more. Stenting was performed evenly across the years.

Tumor location is summarized in Table 1. There were 38 proximal to splenic flexure versus 279 distal tumors (including splenic flexure tumors). Furthermore, 287 tumors (90.0%) were adenocarcinomas. Mucinous adenocarcinoma was the next most common type (n=12, 3.8%). Signet ring adenocarcinoma (n=3), small cell carcinoma (n=2), squamous cell carcinoma (n=1) and neuroendocrine tumor (n=1) were the other subtypes, with 13 patients missing histological subtype data.

Metastatic disease was noted at diagnosis in 57.4% of patients. This was associated with a lower chance of proceeding to an operation (P<0.001). However, there was a survival advantage in proceeding to an operation, even in the presence of metastatic disease (P<0.001) (Table 3). Without an operation, the mean survival was 7.88 months (95% CI, 6.64–9.11) versus 36.43 months with an operation (95% CI, 25.09–47.47). The mortality rate at 5 years in patients with metastatic disease was significantly lower for those who underwent surgery (HR, 0.14; P<0.01). Kaplan-Meier curves show mortality with surgery in various patient groups in Fig. 1.

Stent complications were not recorded, but there were 13 operations performed within 1 week of stent placement (4.08%), with 4 happening on the day of stenting. Twenty-two of 108 patients (20.37%) undergoing surgery in the study were recorded as having a stoma at the end of the study period.

DISCUSSION

This study is one of the largest stenting datasets reported to date, and it is the largest in an Australian population. The indications for stenting were diverse, with both metastatic and localized disease being treated. There was also a survival advantage to undergoing surgery after stenting, even in patients with metastatic disease. Factors favorably influencing long-term survival were as might be expected: patients undergoing subsequent surgery or other treatment (chemotherapy or radiotherapy). Meanwhile, unfavorable survival outcomes were found in patients with metastatic disease and with higher numbers of comorbidities.

There was no influence on survival according to whether patients were from a disadvantaged socioeconomic status, diagnosed in a major city or elsewhere, or treated at private and public hospitals. Importantly this suggests that the treatment of obstructing

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Table 1. Overall demographics, factors affecting stenting as a bridge to surgery, and gastrointestinal continuity

Variable	Overall (n = 319)	Surgery		P-value
		No (n = 211)	Yes (n = 108)	
Mean age (yr)	70.92 ± 14.47	73.16 ± 13.87	66.54 ± 14.70	< 0.001[a]
Sex				0.796
Male	204 (63.9)	133 (63.0)	71 (65.7)	
Female	115 (36.1)	78 (37.0)	37 (34.3)	
Socioeconomic status (n = 318)[b]				0.452
Disadvantaged	70 (22.0)	52 (24.8)	18 (16.7)	
Middle class	207 (65.1)	130 (61.9)	77 (71.3)	
Affluent	41 (12.9)	28 (13.3)	13 (12.0)	
Hospital type				0.126
Public	189 (59.2)	135 (64.0)	54 (50.0)	
Private	130 (40.8)	76 (36.0)	54 (50.0)	
Remoteness (n = 318)[b]				0.616
Major city	221 (69.5)	147 (70.0)	74 (68.5)	
Other	97 (30.5)	63 (30.0)	34 (31.5)	
Comorbidity count (n = 272)[c]				0.876
0–2	201 (73.9)	132 (73.3)	69 (75.0)	
> 3	71 (26.1)	48 (26.7)	23 (25.0)	
ASA PS classification (n = 218)[d]				0.298
0–II (normal or mild disease)	47 (21.6)	25 (18.0)	22 (27.8)	
III–VI (severe disease)	171 (78.4)	114 (82.0)	57 (72.2)	
Diagnosed year				0.389
2008	29 (9.0)	23 (10.9)	6 (5.6)	
2009	49 (15.4)	38 (18.0)	11 (10.2)	
2010	46 (14.4)	29 (13.8)	17 (15.7)	
2011	42 (13.2)	22 (10.4)	20 (18.5)	
2012	52 (16.3)	35 (16.6)	17 (15.7)	
2013	49 (15.4)	30 (14.2)	19 (17.6)	
2014	52 (16.3)	34 (16.1)	18 (16.7)	
Tumor location (n = 317)[e]				0.930
Caecum	1 (0.3)	1 (0.5)	0 (0)	
Ascending colon	8 (2.5)	5 (2.4)	3 (2.8)	
Hepatic flexure	4 (1.3)	4 (1.9)	0 (0)	
Transverse colon	25 (7.9)	18 (8.6)	7 (6.5)	
Splenic flexure	22 (6.9)	14 (6.7)	8 (7.4)	
Descending colon	27 (8.5)	16 (7.6)	11 (10.2)	
Sigmoid colon	152 (48.0)	99 (47.4)	53 (49.1)	
Rectosigmoid	39 (12.3)	25 (12.0)	14 (12.9)	
Rectum	39 (12.3)	27 (12.9)	12 (11.1)	
Disease burden				< 0.001[a]
Nonmetastatic	136 (42.6)	65 (30.8)	71 (65.7)	
Metastatic	183 (57.4)	146 (69.2)	37 (34.3)	
Gastrointestinal continuity	233 (73.0)	211 (100)	86 (79.6)	

Values are presented as mean ± standard deviation or number (%).
ASA, American Society of Anesthesiologists; PS, physical status.
[a]Statistically significant. [b]No surgery, 210 patients; yes surgery, 108 patients. [c]No surgery, 180 patients; yes surgery, 92 patients. [d]No surgery, 139 patients; yes surgery, 79 patients. e No surgery, 209 patients; yes surgery, 108 patients.

Table 2. Cox regression analysis for factors affecting 5-year mortality (n = 319)

Factor	Hazard ratio	95% Confidence interval	P-value
Male sex	1.197	0.880–1.629	0.251
Age (≥ 80 yr)	1.192	0.828–1.714	0.345
Major city	0.718	0.498–1.034	0.075
Hospital type (public vs. private)	1.101	0.814–1.488	0.534
Socioeconomically disadvantaged	0.912	0.604–1.378	0.662
Metastatic disease	2.052	1.418–2.970	< 0.001[a]
Poorly differentiated cancer	1.226	0.830–1.813	0.306
Adenocarcinoma or other	1.299	0.766–2.202	0.332
High ASA PS (III–VI)	1.457	0.987–2.149	0.058
Comorbidity count (> 3)	1.572	1.074–2.301	0.020[a]
Further operation	0.190	0.125–0.288	< 0.001[a]
Chemotherapy, radiotherapy, or both	0.718	0.518–0.994	0.046[a]
Date of diagnosis 2010 onwards	0.730	0.499–1.068	0.104

ASA, American Society of Anesthesiologists; PS, physical status
[a]Statistically significant.

Table 3. Cox regression analysis for factors affecting 5-year mortality in patients with metastatic disease (n = 183)

Factor	Hazard ratio	95% Confidence interval	P-value
Male sex	1.197	0.880–1.629	0.251
Age (≥ 80 yr)	1.192	0.828–1.714	0.345
Major city	0.718	0.498–1.034	0.075
Hospital type (public vs. private)	1.101	0.814–1.488	0.534
Socioeconomically disadvantaged	0.912	0.604–1.378	0.662
Metastatic disease	2.052	1.418–2.970	< 0.001[a]
Poorly differentiated cancer	1.226	0.830–1.813	0.306
Adenocarcinoma or other	1.299	0.766–2.202	0.332
High ASA PS (III–VI)	1.457	0.987–2.149	0.058
Comorbidity count (> 3)	1.572	1.074–2.301	0.020[a]
Further operation	0.190	0.125–0.288	< 0.001[a]
Chemotherapy, radiotherapy, or both	0.718	0.518–0.994	0.046[a]
Date of diagnosis 2010 onwards	0.730	0.499–1.068	0.104

ASA, American Society of Anesthesiologists; PS, physical status
[a]Statistically significant.

CRC, and the use of stenting is equitable in Queensland, despite the geographical challenges over an area greater than 18 times the size of Korea.

In this study, the need for an operation within 7 days was used as a surrogate marker for early stent complications— namely, failure, early re-obstruction, or perforation. This rate was 4.08% (13 of 319). Undergoing surgery within 7 days was associated with an increased risk of 30-day mortality, but did not affect long-term survival. This provides evidence for the long-term safety of stenting, despite the reported early risks in the literature.

The indications for an early operation were not available in this dataset, and it may be that certain indications (e.g., perforation) are associated with worse short- and long-term outcomes. It may also be that this group included those patients with a better underlying prognosis, managed with a bridge to surgery and curative intent. It is interesting that the long-term survival was not affected in the group undergoing early surgery, and it is possible that the small absolute number of early failures was outweighed in 5-year survival by other unaccounted factors, such as tumor biology, comorbidities, and treatment intent.

In this study, the stoma rate was 20.4% for patients who had surgery after stenting (overall rate: 6.9%). Higher stoma rates have been noted in other studies (42.7%–58.7%) [6, 7, 9, 15]. These studies primarily evaluated bridge-to-surgery indications [6, 9, 15], and Borowiec et al. [7], in a population-based study, included an older historical cohort with patients prior to 2010. This sug-

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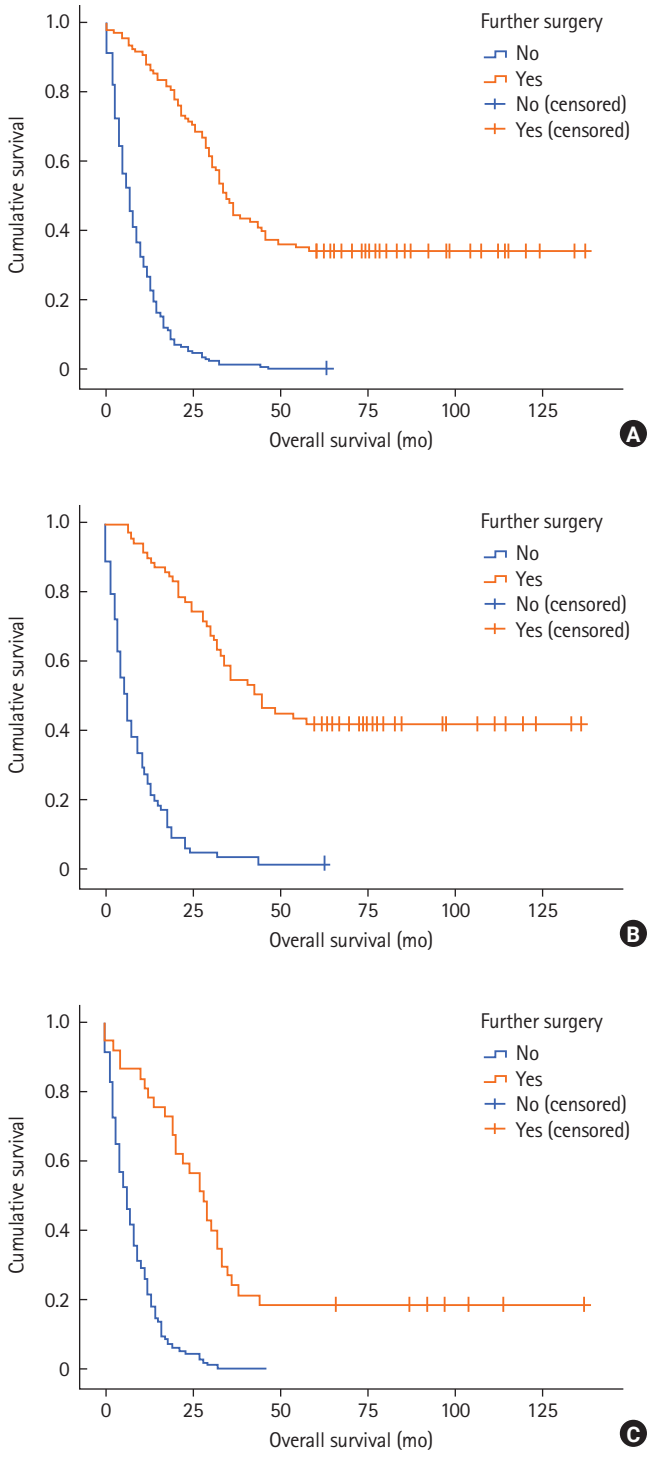

Fig. 1. Kaplan-Meier curves representing surgery poststenting versus no surgery. (A) All patients. (B) Nonmetastatic disease. (C) Patients with metastatic disease.

gests that there is a much lower stoma formation rate after stenting in contemporary cohorts. This supports stenting as both a definitive option and a bridge to surgery, for those patients wishing to avoid a stoma.

Another notable finding was the survival advantage seen in patients undergoing surgery after stenting, even in the presence of metastatic disease. This may reflect improvements in chemotherapy, immunotherapy, and the treatment of metastatic disease. This suggests that even in patients with metastatic disease, stents as a bridge to surgery can be used with careful patient selection. Given the role of stenting to treat obstruction, this modality would reduce the clinical urgency and allow careful consideration of neoadjuvant chemotherapy and possible future operations. This application of stenting certainly merits further research, and population-based datasets provide a snapshot of real-world management decisions and their outcomes.

In 2022, the CReST (Colorectal Endoscopic Stenting Trial) randomized controlled trial [15] supported stenting in the management of left-sided malignant obstruction as a bridge to surgery. For the 119 patients undergoing a colonic stent placement, the 30-day mortality rate was 3.6%. This compares favorably with the present study's 6.6% 30-day mortality rate. The stenting group in the CReST trial was mainly considered curative (110 of 123, 89.43%), with only 17.1% patients (21 of 123) having metastatic disease at randomization. The ASA PS in the group were also low, with 82.9% of patients having grades of I to II. In contrast, the present study included patients in whom stenting was definitive palliative management— both due to disease burden (metastases in 57.4%) and comorbidities (ASA PS >II in 78.4%)—and this may have contributed to the higher observed 30-day mortality rate. This is likely reflected in the 3-year mortality rate of 40% in the CReST trial, versus a substantially higher 82.8% in the present study. However, in a subgroup analysis (patients with nonmetastatic disease and with an ASA PS <3), the 3-year mortality rate in this study dropped to equivalent levels (8 of 21, 38.1%). The 1-year stoma rate in the CReST trial was 44.5%. Four patients in the CReST trial had a stent-related perforation (3.3%), and a further 4 patients experienced obstruction within a week. The present study observed similar proportions of stented patients who returned to theatre within a week of stenting for any reason (13 patients, 4.1%).

Padwick et al. [16] published a smaller (n=89) observational study based over a 10-year period in 2016. This was focused on a single UK tertiary referral center. The 30-day mortality rate in this study was 4.49% (vs. 6.6% in the present study), with a median survival of 6.04 months (vs. 11 months in our study).

The present study captures all stenting performed in Queensland for obstructing CRC. The mandatory reporting by law of all can-

cers to the QCR means that this is a truly population-based cohort and is a substantial strength of the study. This is a true representation of the treatment offered to patients across Queensland over the 7-year study period. It does not center around a single tertiary referral center and the highly specialized and selected consequent cohorts.

Nonetheless, there are limitations to this study. The data are not as granular as data from a single center. As such, the precise indication or intent of stenting was unknown. Comorbidity data could not be accessed for 47 patients, but there was a high level of data completeness otherwise. Stent-related complications were inferred by an early operation in the first 7 days after stenting, but there may have been cases where an early operation was deliberately planned in the first week after stenting.

In conclusion, this large population-based study adds to the literature by presenting real-world data supporting the use of expanding metal stents in obstructing CRC. It supports the use of stenting in the treatment paradigm.

ARTICLE INFORMATION

Conflict of interest
No potential conflict of interest relevant to this article was reported.

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Author contributions
Conceptualization: CK, DAC; Data curation: JM, DC, CK; Formal analysis: CK; Investigation: CK; Methodology: CK, NS, DAC; Project administration: CK, JM, DC, DAC; Visualization: CK, DAC; Writing–original draft: CK; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Additional information
This study was presented at the Royal Australasian College of Surgeons (RACS) Annual Scientific Congress in March 2022, in Brisbane, Australia.

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