

Role of surgery for colorectal cancer in the elderly

Antonio Biondi, Marco Vacante, Immacolata Ambrosino, Erika Cristaldi, Giuseppe Pietrapertosa, Francesco Basile

Antonio Biondi, Francesco Basile, Department of Surgery, Vittorio Emanuele Hospital, University of Catania, 95100 Catania, Italy

Marco Vacante, Erika Cristaldi, Department of Medical and Pediatric Sciences, University of Catania, 95100 Catania, Italy

Immacolata Ambrosino, Giuseppe Pietrapertosa, Community Hospital Service ULSS 20 Verona, 37122 Verona, Italy

Author contributions: All authors wrote and critically revised the manuscript.

Conflict-of-interest statement: No potential conflicts of interest relevant to this article were reported.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Antonio Biondi, MD, PhD, Associate Professor, Department of Surgery, Vittorio Emanuele Hospital, University of Catania, Via Plebiscito 628, 95100 Catania, Italy. abiondi@unict.it
Telephone: +39-95-7435373

Received: March 25, 2016

Peer-review started: March 25, 2016

First decision: May 23, 2016

Revised: June 15, 2016

Accepted: July 14, 2016

Article in press: July 18, 2016

Published online: September 27, 2016

Abstract

The prevalence of subjects with colorectal cancer is expected to grow in the next future decades and surgery represents the most successful treatment modality for these patients. Anyway, currently elderly subjects undergo less elective surgical procedures than younger patients mainly due to the high rates of postoperative morbidity and mortality. Some authors suggest extensive surgery, including multistage procedures, as carried out in younger patients while others promote less aggressive surgery. In older patients, laparoscopic-assisted colectomy showed a number of advantages compared to conventional open surgery that include lower stress, higher rate of independency after surgery, quicker return to prior activities and a decrease in costs. The recent advances in chemotherapy and the introduction of new surgical procedures such as the endoluminal stenting, suggest the need for a revisitation of surgical practice patterns and the role of palliative surgery, mainly for patients with advanced disease. In this article, we discuss the current role of surgery for elderly patients with colorectal cancer.

Key words: Laparoscopy; Colorectal cancer; Elderly; Comorbidities; Colorectal surgery

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Age itself should not be considered as a risk factor for the development of complications in patients undergoing surgery for colorectal cancer. Many studies underlined that age is not a predictor of post operative complications in these patients. Therapeutic or palliative surgery should not be avoided in the elderly based exclusively on age.

Biondi A, Vacante M, Ambrosino I, Cristaldi E, Pietrapertosa G, Basile F. Role of surgery for colorectal cancer in the elderly. *World J Gastrointest Surg* 2016; 8(9): 606-613 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v8/i9/606.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v8.i9.606>

INTRODUCTION

Colorectal cancer (CRC) represents the third most commonly diagnosed cancer in developed countries, with almost 694000 deaths estimated to have occurred in 2012^[1]. The prevalence of elderly subjects with CRC is expected to grow in the next future decades due to the increase of age in the general population^[2]. In fact, CRC is infrequently diagnosed before age of 40, with a highest risk around age of 70.75% of CRC are identified in patients aged 65 years or older^[3]. In both Europe and United States approximately 50% of CRC patients are older than 70 years of age and in this age group CRC is the second most common cause of cancer death^[4,5]. Thus, age could be considered as a major risk factor for the development of this cancer^[6].

Many studies showed that surgical approach represents the most successful treatment modality for patients with CRC. Over the past years it has been observed an improvement in the survival of subjects with this cancer mainly due to a reduction in operative mortality and a raising in the resection rate^[7]. However, there is significant evidence that elderly subjects undergo less elective surgical procedures than younger patients^[8] mainly due to the high rates of postoperative morbidity and mortality^[9].

IMPACT OF AGE ON CRC SURGERY

There is a lack of consensus on the impact of age on postoperative outcome after major colorectal surgery. In fact, comorbidities are higher in elderly subjects thus leading to difficult decisions whether these patients are suitable for extensive bowel resection or not. A review of the literature published in the *Lancet* in 2000 pointed out that elderly patients are less likely to have curative surgery than younger patients^[8].

In 2008, the International Society of Geriatric Oncology (SIOG) created a task force to develop guidelines for the treatment of elderly patients with CRC^[10]. The task force confirmed the paucity of clinical trial data in the elderly and pointed out that treatment for elderly CRC patients should be analogous to those of younger patients.

A registry-based study carried out by Damhuis *et al*^[9] on 6457 patients with CRC, evaluated the influence of age and other variables on resection rates and operative risk. All subjects included in the study were enrolled from 1985 through 1992 in hospitals connected to the Rotterdam Cancer Registry. Data analysis showed that 87% of the patients underwent resection but resection

rates were lower for patients older than 89 years (67%) and for patients with rectal cancer (83%). Patients younger than 60 years had a postoperative mortality rate of 1% that constantly increased with age. Patients 80 years and older showed an operative risk of 10%. Multivariate analysis was conducted and pointed out that gender, age, cancer subsite and stage could be considered as independent prognostic factors. The authors concluded that chronological age alone should not be an exclusion criteria for performing surgery in elderly patients with CRC. Even in patients aged over 90 years, resections can be performed with acceptable risk.

Another study^[11] analysed the electronic records from the Rotterdam Cancer Registry for octogenarians and nonagenarians who underwent resection in the period 1987-2000. The results showed that for CRC, postoperative mortality rates increased from 8% in patients aged 80 to 84 years, to 13% in patients aged 85 to 89 years and to 20% in nonagenarians.

A systematic review of 28 independent studies and 34194 patients, carried out by the Colorectal Cancer Collaborative Group, analysed the results for different groups of patients aged 65-74 years, 75-84 years and 85+ years with those for patients aged < 65 years. Compared with younger subjects, elderly patients have an increased frequency of comorbid conditions, are more likely to present with later-stage disease and undergo emergency surgery^[8]. Moreover, many studies focused on the role of adjuvant chemotherapy, demonstrating that elderly are less likely to be recommended or to receive adjuvant treatment^[12].

COMORBIDITIES AND COMPLICATIONS

Traditionally, contraindications for major surgery in elderly patients include a poor functional status, associated comorbidities and impaired cognition^[13]. Anyway, in the last 30 years elderly patients with CRC took advantage of healthcare progress and a retrospective trend analysis showed a reduction of palliative procedures and a decline in operative mortality for these patients^[14].

Most elderly patients with CRC have significant comorbidities such as cardiovascular and pulmonary diseases. Such diseases increase the operative risk and the risk of postoperative morbidity and mortality^[15,16]. A study by Hermans *et al*^[17] evaluated the impact of comorbidities on the outcome of colonic surgery in elderly patients with colon cancer.

Comorbid assessment tools provide helpful information on the impact of comorbidities at the initial diagnosis and prospective outcome of CRC patients due to their prognostic capacity on survival. According to the classification of Charlson *et al*^[18], the evaluated comorbidities included previous malignancies, chronic obstructive pulmonary disease, cardiovascular disease, cerebrovascular disease, hypertension, diabetes, and others (rheumatoid arthritis, hyperthyroidism, hypothyroidism, and sclerodermia). Compared to younger

age, elderly subjects presented with more cardiovascular pathology and dementia and with more than one type of the previously described comorbidities. The authors concluded that the type and number of co-morbidities influence post-operative mortality and morbidity. Complications were seen in 24% of younger patients vs 50% of elderly patients. No difference was observed as regards major complications (e.g., anastomotic leakage, fascia dehiscence, or intra-abdominal abscesses). In the elderly group there was a high incidence of delirium, pneumonia, wound infections, and minor complications such as urinary tract infection, and electrolyte alterations. Other factors that may cause poor outcome of surgery in the elderly include delayed presentation and advanced stage of the disease^[19,20].

As regards preoperative factors that could influence the choice of treatment, Marventano *et al.*^[19] proposed a modified version of the Charlson comorbidity index (CCI) that was specifically developed for colorectal cancer patients. This version of CCI emphasized the importance of specific conditions to better predict the survival of the patients. Particularly, the inclusion of 6-mo weight loss $\geq 20\%$, smoking > 20 cigarettes/d, underweight condition, and cardiac arrhythmias to the other comorbid conditions tested in the CCI showed a better predictive value compared with the original CCI and other comorbidity indices (e.g., the Elixhauser method, the National Institute on Aging and National Cancer Institute comorbidity index, and the Adult Comorbidity Evaluation-27). Noteworthy, the Authors found that only moderate or severe renal disease and diagnosis of AIDS were independently associated with higher risk of death^[19].

An analysis of 31574 patients in the surveillance, epidemiology and end results-medicare database for patients diagnosed with colon cancer between 1992 and 2005 was conducted to describe patterns of surgery in patients aged > 80 years and examine outcomes with and without colectomy. The Authors demonstrated that 80% of the "oldest old" patients with colon cancer in the United States are undergoing surgical resection^[21]. In this study, 46% of subjects were diagnosed during an urgent or emergent hospital admission, with decreased 1-year overall survival (70% vs 86% for patients diagnosed during an elective admission). Older age, black race, more hospital admission, use of home oxygen, use of wheelchair, frailty and dementia were most predictive of nonoperative management. The 1-year overall survival rate for both operative and nonoperative patients was lower than the colon cancer-specific survival rate (operative patients: 78% vs 89%; nonoperative patients: 58% vs 78%)^[21].

A study by Kahn *et al.*^[22] showed that older age is not independently associated with complications after surgery for colorectal cancer. The Authors underlined the importance of clinical status and American Society of Anesthesiologists (ASA) class in patients' selection rather than age.

THERAPEUTIC OPTIONS FOR CRC IN THE ELDERLY

Different approaches to treat elderly subjects with CRC have been proposed over the past years. Some authors endorse extensive surgery, including multistage procedures, as carried out in younger patients^[23,24], while others promote less aggressive surgery^[25,26].

Most subjects with stage I or II CRC are treated by surgery, even if some patients with stage II could benefit from adjuvant therapy^[27,28]. Surgery followed by adjuvant chemotherapy is the standard treatment for stage III CRC. Subjects with metastases could benefit from chemotherapy alone or combined with targeted therapy. At this stage, surgery is indicated in selected patients. The treatment for stage IV CRC includes surgery and preoperative or postoperative, radiotherapy and/or chemotherapy.

Different factors could influence surgical outcomes in stage IV CRC, including the presence of liver metastases^[29,30] and cardiovascular disease^[31], the degree of peritoneal involvement and primary cancer resection^[32], the tumor differentiation, and age older than 75^[33].

There is still uncertainty about the effective benefit of surgery directed toward removal of the primary tumor for the management of asymptomatic patients with stage IV CRC and unresectable metastases. Palliative surgery is indicated for most patients with bowel obstruction or uncontrollable bleeding^[34].

Guidelines from the National Comprehensive Cancer Network recommend surgical treatment in stage IV CRC only in symptomatic patients at risk of obstruction, or with metastases suitable for potentially curative resection^[35].

A study by Temple *et al.*^[34] evaluated surgical practice patterns for patients over 65 years of age with stage IV CRC in a United States population-based cohort. They observed that 72% of patients received primary-cancer-directed surgery (CDS) with a 30-d postoperative mortality of 10%. CDS was less performed on patients with left-sided or rectal lesions, subjects older than 75 years, blacks, and those of lower socioeconomic status; but even among those older than age 75, the CDS rate was 69%. Chemotherapy was administered to 47% of patients that underwent CDS vs 31% of patients who did not. The resection of metastases was performed only on 3.9% of patients at any point from diagnosis to death^[34].

There is evidence that subjects with stage IV CRC could tolerate chemotherapy without requiring surgery to remove the primary tumor. In fact, a study by Tebbutt *et al.*^[36] showed that there were no differences in gastrointestinal complications (e.g., fistulas, peritonitis, obstruction) in patients who did not undergo CDS compared to those who had CDS^[36]. The recent advances in chemotherapy and the introduction of new surgical procedures (e.g., endoluminal stenting) suggest the need for a revisitation of surgical practice patterns and the role of palliative surgery for IV stage CRC patients.

Many studies underlined the importance of laparoscopic assisted colectomy (LAC) for the treatment of CRC. However the majority of them were conducted on patients younger than 65 years. In general, LAC showed a number of advantages compared to conventional open surgery that include lower stress, higher rate of independency after surgery, quicker return to prior activities and a decrease in costs^[37,38].

There are many issues related to the limited number of LAC carried out on elderly subjects requiring colectomy: First of all, the high number of comorbidities; second, the longer operative times; and third, the paucity of scientific literature assessing risks and benefits of this procedure in the elderly. A review of the literature carried out by Mutch^[37] identified 18 studies on LAC in the elderly. There is significant evidence that LAC could be performed in the elderly population safely and without significant increase in morbidity and mortality^[38].

A study by Vara-Thorbeck *et al.*^[39] represents the first report of LAC in older patients. The study was conducted on 18 patients that underwent LAC for CRC. Eleven subjects were older than 70 years. None of the cases were converted to open laparotomy, and the mortality was null. The results showed that LAC could be performed safely on both older and younger patients while maintaining the same principles of surgical technique as open colectomy. A number of more recent studies confirmed that laparoscopy-assisted colectomy in the elderly can be performed with no difference in morbidity or length of hospital stay compared with open surgery^[40-44]. Vignali *et al.*^[45], compared the outcomes of open colectomy vs LAC in a population of octogenarians. They observed that the patients undergoing LAC had a shorter hospital stay (LAC 9.8 d vs open 12.9 d), reduced morbidity (LAC 21% vs open 31%), and higher rate of independence at discharge (LAC 98% vs open 82%), thus confirming that the benefits of LAC are maintained with advancing age.

A study by Bardram *et al.*^[46] analyzed the outcomes of laparoscopy combined with a perioperative multimodal rehabilitation protocol in 50 patients of median age 81 years. After LAC, patients were treated with epidural local anaesthesia for 2 d, early mobilization and oral nutrition, with a significant improvement in recovery.

O'Connell *et al.*^[47] pointed out that in frail elderly with limited life expectancy, the benefits of cancer surgery are frequently unclear, and surgical resection of tumors is less performed as the patient ages.

A study by Finlayson *et al.*^[48] aimed to determine functional status and mortality rates after colon cancer surgery in older nursing home residents. They conclude that even when not curative, surgery for CRC may be an effective palliative procedure. Less invasive treatments, such as endoscopic treatment or embolization of bleeding tumors or the use of endoluminal stents for large bowel obstruction, may represent an alternative to surgery for individuals with limited life expectancy.

The international SIOG expert recommendations, according to the available evidence on CRC in the elderly, suggested that emergency surgery should be avoided

when possible; the use of colorectal stents should be taken into account to improve patient nutrition thus facilitating elective surgery 1-2 wk after the patient has presented as an emergency; the pathway of choice should be elective surgery with a prospective analysis of the perioperative variables and careful treatment; possible curative resection of liver metastases should be performed in healthy elderly subjects receiving a careful preoperative assessment and a high quality postoperative care^[10].

As regards rectal cancer, analysis of 991 treatments, in the 838 elderly rectal cancer patients from the Cote d'Or and Calvados tumor registries study^[49], showed 54% of patients to undergo curative resection, 7% to undergo palliative resection, 12% to undergo by-pass laparotomy, 27% to undergo no surgery, 17% to receive radiotherapy and 2% to receive chemotherapy. These data highlighted a low use of radiotherapy either combined with surgery or alone, while chemotherapy was almost never administered. Both surgery and radiotherapy are important for controlling local recurrence and therefore local failure rates. Recently the use of the surgical technique total mesorectal excision^[50] has contributed to a reduction in pelvic recurrences. A study by Kim *et al.*^[51] assessed the long-term oncological and functional outcomes of intersphincteric resection for T2 and T3 low rectal cancer. The authors observed a 5-year overall survival rates of 95.8% for T2 and of 94.7% for T3. The 5-year recurrence-free survival rates were 87.5% for T2 and 86.8% for T3 (Table 1). Radiotherapy has been shown to impact significantly on survival in resectable tumors^[52] and is critical for the management of patients with all stages of rectal tumors.

CONCLUSION

In general, there are age-related disparities in colon cancer treatment, with older patients being less likely to receive recommended therapy. According to the SIOG guidelines, elderly subjects should receive screening and earlier diagnosis; the management of CRC should be more aggressive and closer to that received by younger patients; the treatment should be the most intensive and appropriate according to the biological age and the presence of comorbidities^[10]. Many studies pointed out that age is not a predictor of post operative complications in patients with CRC^[53-56]. Age itself should not be considered as a risk factor for the development of complications in patients undergoing surgery for CRC. Thus, therapeutic or palliative surgery based solely on age should not be avoided in these patients. In the future, the surgical assessment of CRC in the elderly should take into account a multidisciplinary process before choosing the best possible therapy for each patient. There will be the need for services specialized in the care of at-risk older patients, rehabilitation and palliative care consultation. An appropriate management should also include the functional status, the grade of frailty, the life expectancy and also patient's requests.

Ref.	Year	No. of patients	Postoperative mortality	Resection rates	Comorbidities	Survival rate	Independent prognostic factors
Damhuis <i>et al</i> ⁽⁹⁾	1996	6457	1% for patients < 60 yr and steadily increased with age. The operative risk was 10% for patients > 80 yr	87% of the patients underwent resection. 67% for patients > 89 yr and 83% for patients with rectal cancer	-	-	Gender, age, subsite and stage
Damhuis <i>et al</i> ⁽¹¹⁾	2005	2765	Increased from 8% for the age group 80-84 to 13% for those 85-89 to 20% in nonagenarian	-	-	-	-
Hermans <i>et al</i> ⁽⁷⁾	2010	207	In-hospital mortality was 16% in the elderly and 5% in the younger group ($P < 0.01$)	No differences between < 75 yr and > 75 yr: ileocecal resection (2% vs 4%); hemicolectomy right (42% vs 49%); transversum resection (1% vs 3%); hemicolectomy left (15% vs 8%); sigmoid resection (26% vs 22%); anterior resection (10% vs 9%); subtotal colectomy (3% vs 1%); double resection (1% vs 4%)	More co-morbidities > 75 yr, especially cardiovascular pathology ($P < 0.01$) and dementia ($P < 0.01$), more than one type of comorbidity according to the Charlson classification ($P < 0.05$)	5-yr survival rate in < 75 yr was 62% compared with 36% in the elderly ($P < 0.05$)	-
Neuman <i>et al</i> ⁽²¹⁾	2013	31574	30-d mortality rate of 10% after urgent/emergent admission	-	Hypertension, peripheral vascular disease, and chronic pulmonary disease were found to be associated with improved overall and cancer-specific survival	The 1-yr overall survival rate was lower than the colon cancer-specific survival rate (operative patients: 78% vs 89%, non-operative patients: 56% vs 76%)	Older age, black race, more hospital admissions, use of home oxygen, use of a wheelchair, being frail, and having dementia
Irvin ⁽²¹⁾	1988	306	The surgical mortality rates for patients > 70 yr were 6% overall, 4% after elective operations, and 16% after emergency surgery; the corresponding mortality rates for patients < 70 yr were 3%, 1%, and 20%	-	-	Crude actuarial 5-yr survival curves showed an increased death rate for patients > 70 yr after 18 mo and a significantly lower 5-yr survival ($P < 0.05$) but the age-corrected survival curves for the two groups were not significantly different	-
Temple <i>et al</i> ⁽³⁴⁾	2004	9011	The 30-d postoperative mortality was 10%. The 30-d surgical mortality was significantly greater in the no primary cancer-directed surgery (CDS) group among patients who underwent a surgical procedure, when compared with the primary CDS group (26% vs 9%, $P = 0.001$)	The rates of CDS declined with age: 76% of 65 to 69-yr-old patients received primary CDS, whereas the rate declined to 62% of patients age ≥ 85 yr	-	The overall median survival for the entire cohort was 7 mo. There were differences in survival between patients treated with CDS and no CDS exist (median, 10 mo vs 3 mo, respectively), but data are not reliably because of patient selection in the non-randomized setting	Left-sided or rectal lesions, age > 75 yr, blacks, marital status and lower socioeconomic status
Vallribera Valls <i>et al</i> ⁽⁴²⁾	2014	277: Laparoscopic group; 268: Open group	Open surgery group showed a higher mortality (6.7% vs 3.2%, $P = 0.034$). Mortality was significantly inferior in laparoscopy group in younger patients (< 75 yr, 0% vs 3%, $P = 0.038$)	-	Open surgery group showed a higher overall morbidity rate (37.3 vs 21.6%, $P = 0.001$), medical complications (16.4% vs 10.5%, $P = 0.033$), surgical complications (23.5% vs 15.5%, $P = 0.034$), the	-	-

Author	Year	Study Design	Population	Intervention	Comparison	Results	Conclusions
Vignali <i>et al</i> ^[45]	2005	61: Laparoscopic colectomy; 61: Open colectomy	Overall mortality rate was 2.4%. The morbidity rate was 21.5% in the laparoscopy group and 31.1% in the open group ($P = 0.30$)	Overall mortality rate was 2.4%. The morbidity rate was 21.5% in the laparoscopy group and 31.1% in the open group ($P = 0.30$)	-	Overall morbidity rate difference between open and laparoscopy approach disappeared in the oldest group (≥ 85 yrs old). Surgical site infections rate was inferior for patients < 75 yr old in laparoscopy group compared with open	-
Bouvier <i>et al</i> ^[46]	2005	1571 with colon cancer; 838 with rectal cancer	During the study period from 8.7% to 9.5% for colon and from 16.3% to 5.6% for rectum	69% in colon cancer; 54% in rectal cancer	-	Overall 3-yr survival rates were 45.2% for colon cancer and 46.2% for rectal cancer. Overall 5-yr survival rates were 40.9% and 37.3% respectively	Age, gender, period of diagnosis, treatment. A second multivariate analysis restricted to patients resected for cure and alive after the first month of follow-up showed that age between 85 and 89 was no longer a significant factor of survival
Heald <i>et al</i> ^[50]	1998	519 with rectal cancer	The operative mortality (30-d) was 3.3%	-	-	68% at 5 yr and 66% at 10 yr	-
Kim <i>et al</i> ^[51]	2016	62 with very low rectal cancer. Group I, $n = 24$, stage T2. Group II, $n = 38$, stage T3	No postoperative mortality in both groups	Temporary urinary retention (group I : 10 cases; Group II : 15 cases), postoperative paralytic ileus (group I : 2 cases; Group II : 3 cases), perineal abscess (group I : 1 case; Group II : 1 case), and anastomotic leakage (group I : 1 case; Group II : 1 case). Late complications, such as anastomotic stricture (group I : 6 cases; Group II : 10 cases), rectovaginal fistula (group I : 0 case; Group II : 1 case) after stoma closure	-	5-yr overall survival rates were 95.8% for group I and 94.7% for group II. The 5-yr recurrence-free survival rates were 87.5% for group I and 86.8% for group II	-
Schiffmann <i>et al</i> ^[54]	2008	517	30-d mortality was higher in the older age group (> 75 yr)	-	-	No differences in 30-d morbidity except in postoperative bleeding	-
Devon <i>et al</i> ^[55]	2009	898	The in-hospital mortality rate was 1% in the younger group (< 75 yr) compared with 4.2% in the older (> 75 yr) ($P = 0.002$)	-	-	The overall five-year survival was 68.7% and 57.3% in the younger and older groups, respectively, whereas colorectal cancer-specific five-year survival was not significantly different (74.0% vs 74.7%)	-
Paksoy <i>et al</i> ^[56]	1999	822	The postoperative (30 d) mortality was 3% in the younger group (< 65 yr) (20/565) and 7% in the older group (17/257) (difference not significant)	-	-	Five-year survival rates for older and younger patients were 33% and 45%, respectively ($P < 0.05$)	-

REFERENCES

- 1 **Torre LA**, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin* 2015; **65**: 87-108 [PMID: 25651787 DOI: 10.3322/caac.21262]
- 2 **Mäkelä JT**, Kiviniemi H, Laitinen S. Survival after operations for colorectal cancer in patients aged 75 years or over. *Eur J Surg* 2000; **166**: 473-479 [PMID: 10890544 DOI: 10.1080/110241500750008790]
- 3 **Greenlee RT**, Hill-Harmon MB, Murray T, Thun M. Cancer statistics, 2001. *CA Cancer J Clin* 2001; **51**: 15-36 [PMID: 11577478 DOI: 10.3322/canjclin.51.1.15]
- 4 **Folprecht G**, Cunningham D, Ross P, Glimelius B, Di Costanzo F, Wils J, Scheithauer W, Rougier P, Aranda E, Hecker H, Köhne CH. Efficacy of 5-fluorouracil-based chemotherapy in elderly patients with metastatic colorectal cancer: a pooled analysis of clinical trials. *Ann Oncol* 2004; **15**: 1330-1338 [PMID: 15319237 DOI: 10.1093/annonc/mdh344]
- 5 **Grosso G**, Biondi A, Galvano F, Mistretta A, Marventano S, Buscemi S, Drago F, Basile F. Factors associated with colorectal cancer in the context of the Mediterranean diet: a case-control study. *Nutr Cancer* 2014; **66**: 558-565 [PMID: 24754383 DOI: 10.1080/01635581.2014.902975]
- 6 **de Rijke JM**, Schouten LJ, Hillen HF, Kiemeny LA, Coebergh JW, van den Brandt PA. Cancer in the very elderly Dutch population. *Cancer* 2000; **89**: 1121-1133 [PMID: 10964343 DOI: 10.1002/1097-0142(20000901)89]
- 7 **Marventano S**, Forjaz M, Grosso G, Mistretta A, Giorgianni G, Platania A, Gangi S, Basile F, Biondi A. Health related quality of life in colorectal cancer patients: state of the art. *BMC Surg* 2013; **13** Suppl 2: S15 [PMID: 24267735 DOI: 10.1186/1471-2482-13-S2-S15]
- 8 Surgery for colorectal cancer in elderly patients: a systematic review. Colorectal Cancer Collaborative Group. *Lancet* 2000; **356**: 968-974 [PMID: 11041397 DOI: 10.1016/S0140-6736(00)02713-6]
- 9 **Damhuis RA**, Wereldsma JC, Wiggers T. The influence of age on resection rates and postoperative mortality in 6457 patients with colorectal cancer. *Int J Colorectal Dis* 1996; **11**: 45-48 [PMID: 8919342]
- 10 **Papamichael D**, Audisio R, Horiot JC, Glimelius B, Sastre J, Mity E, Van Cutsem E, Gosney M, Köhne CH, Aapro M. Treatment of the elderly colorectal cancer patient: SIOG expert recommendations. *Ann Oncol* 2009; **20**: 5-16 [PMID: 18922882 DOI: 10.1093/annonc/mdn532]
- 11 **Damhuis RA**, Meurs CJ, Meijer WS. Postoperative mortality after cancer surgery in octogenarians and nonagenarians: results from a series of 5,390 patients. *World J Surg Oncol* 2005; **3**: 71 [PMID: 16280074 DOI: 10.1186/1477-7819-3-71]
- 12 **Krzyzanowska MK**, Regan MM, Powell M, Earle CC, Weeks JC. Impact of patient age and comorbidity on surgeon versus oncologist preferences for adjuvant chemotherapy for stage III colon cancer. *J Am Coll Surg* 2009; **208**: 202-209 [PMID: 19228531 DOI: 10.1016/j.jamcollsurg.2008.10.016]
- 13 **Janssen-Heijnen ML**, Maas HA, Houterman S, Lemmens VE, Rutten HJ, Coebergh JW. Comorbidity in older surgical cancer patients: influence on patient care and outcome. *Eur J Cancer* 2007; **43**: 2179-2193 [PMID: 17681780 DOI: 10.1016/j.ejca.2007.06.008]
- 14 **Nascimbeni R**, Di Fabio F, Di Betta E, Salerno B. The changing impact of age on colorectal cancer surgery. A trend analysis. *Colorectal Dis* 2009; **11**: 13-18 [PMID: 18294264 DOI: 10.1111/j.1463-1318.2008.01491.x]
- 15 **De Marco MF**, Janssen-Heijnen ML, van der Heijden LH, Coebergh JW. Comorbidity and colorectal cancer according to subsite and stage: a population-based study. *Eur J Cancer* 2000; **36**: 95-99 [PMID: 10741301 DOI: 10.1016/S0959-8049(99)00221-X]
- 16 **Grosso G**, Biondi A, Marventano S, Mistretta A, Calabrese G, Basile F. Major postoperative complications and survival for colon cancer elderly patients. *BMC Surg* 2012; **12** Suppl 1: S20 [PMID: 23173563 DOI: 10.1186/1471-2482-12-S1-S20]
- 17 **Hermans E**, van Schaik PM, Prins HA, Ernst MF, Dautzenberg PJ, Bosscha K. Outcome of colonic surgery in elderly patients with colon cancer. *J Oncol* 2010; **2010**: 865908 [PMID: 20628482 DOI: 10.1155/2010/865908]
- 18 **Charlson ME**, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373-383 [PMID: 3558716 DOI: 10.1016/0021-9681(87)90171-8]
- 19 **Marventano S**, Grosso G, Mistretta A, Bogusz-Czerniewicz M, Ferranti R, Nolfo F, Giorgianni G, Rametta S, Drago F, Basile F, Biondi A. Evaluation of four comorbidity indices and Charlson comorbidity index adjustment for colorectal cancer patients. *Int J Colorectal Dis* 2014; **29**: 1159-1169 [PMID: 25064390 DOI: 10.1007/s00384-014-1972-1]
- 20 **Scott NA**, Jeacock J, Kingston RD. Risk factors in patients presenting as an emergency with colorectal cancer. *Br J Surg* 1995; **82**: 321-323 [PMID: 7795995 DOI: 10.1002/bjs.1800820311]
- 21 **Neuman HB**, O'Connor ES, Weiss J, Loconte NK, Greenblatt DY, Greenberg CC, Smith MA. Surgical treatment of colon cancer in patients aged 80 years and older: analysis of 31,574 patients in the SEER-Medicare database. *Cancer* 2013; **119**: 639-647 [PMID: 22893570 DOI: 10.1002/cncr.27765]
- 22 **Kahn KL**, Adams JL, Weeks JC, Chrischilles EA, Schrag D, Ayanian JZ, Kiefe CI, Ganz PA, Bhoopalam N, Potosky AL, Harrington DP, Fletcher RH. Adjuvant chemotherapy use and adverse events among older patients with stage III colon cancer. *JAMA* 2010; **303**: 1037-1045 [PMID: 20233821 DOI: 10.1001/jama.2010.272]
- 23 **Irvin TT**. Prognosis of colorectal cancer in the elderly. *Br J Surg* 1988; **75**: 419-421 [PMID: 3390669 DOI: 10.1002/bjs.1800750508]
- 24 **Wobbes T**. Carcinoma of the colon and rectum in geriatric patients. *Age Ageing* 1985; **14**: 321-326 [PMID: 4072820 DOI: 10.1093/ageing/14.6.321]
- 25 **Greenburg AG**, Saik RP, Pridham D. Greenburg AG, Saik RP, Pridham D. Influence of age on mortality of colon surgery. *Am J Surg* 1985; **150**: 65-70 [PMID: 4014573 DOI: 10.1016/0002-9610(85)90011-X]
- 26 **Violi V**, Pietra N, Grattarola M, Sarli L, Choua O, Roncoroni L, Peracchia A. Curative surgery for colorectal cancer: long-term results and life expectancy in the elderly. *Dis Colon Rectum* 1998; **41**: 291-298 [PMID: 9514423 DOI: 10.1007/BF02237482]
- 27 **André T**, Boni C, Mounedji-Boudiaf L, Navarro M, Taberno J, Hickish T, Topham C, Zaninelli M, Clingan P, Bridgewater J, Tabah-Fisch I, de Gramont A. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med* 2004; **350**: 2343-2351 [PMID: 15175436 DOI: 10.1056/NEJMoa032709]
- 28 **André T**, Tournigand C, Achille E, Tubiana-Mathieu N, Lledo G, Raoul Y, Carola E, Flesch M, Muron T, Boutan-Laroze A, Guérin Meyer V, Boaziz C, Maigre M, Ganem G, Mousseau M, Mounedji-Boudiaf L, de Gramont A. [Adjuvant treatment of colon cancer MOSAIC study's main results]. *Bull Cancer* 2006; **93** Suppl 1: S5-S9 [PMID: 16483940]
- 29 **Liu SK**, Church JM, Lavery IC, Fazio VW. Operation in patients with incurable colon cancer--is it worthwhile? *Dis Colon Rectum* 1997; **40**: 11-14 [PMID: 9102251 DOI: 10.1007/BF02055675]
- 30 **Biondi A**, Tropea A, Basile F. Clinical rescue evaluation in laparoscopic surgery for hepatic metastases by colorectal cancer. *Surg Laparosc Endosc Percutan Tech* 2010; **20**: 69-72 [PMID: 20393330 DOI: 10.1097/SLE.0b013e3181d83f02]
- 31 **Ruo L**, Gougoutas C, Paty PB, Guillem JG, Cohen AM, Wong WD. Elective bowel resection for incurable stage IV colorectal cancer: prognostic variables for asymptomatic patients. *J Am Coll Surg* 2003; **196**: 722-728 [PMID: 12742204 DOI: 10.1016/S1072-7515(03)00136-4]
- 32 **Rosen SA**, Buell JF, Yoshida A, Kazsuba S, Hurst R, Michelassi F, Millis JM, Posner MC. Initial presentation with stage IV colorectal cancer: how aggressive should we be? *Arch Surg* 2000; **135**: 530-534; discussion 534-535 [PMID: 10807276 DOI: 10.1001/arc surg.135.5.530]
- 33 **Joffe J**, Gordon PH. Palliative resection for colorectal carcinoma. *Dis Colon Rectum* 1981; **24**: 355-360 [PMID: 6167412 DOI: 10.1007/BF02603417]

- 34 **Temple LK**, Hsieh L, Wong WD, Saltz L, Schrag D. Use of surgery among elderly patients with stage IV colorectal cancer. *J Clin Oncol* 2004; **22**: 3475-3484 [PMID: 15337795 DOI: 10.1200/JCO.2004.10.218]
- 35 National Comprehensive Cancer Network: Clinical Practice Guidelines. Available from: URL: https://www.nccn.org/professionals/physician_gls/f_guidelines.asp
- 36 **Tebbutt NC**, Norman AR, Cunningham D, Hill ME, Tait D, Oates J, Livingston S, Andreyev J. Intestinal complications after chemotherapy for patients with unresected primary colorectal cancer and synchronous metastases. *Gut* 2003; **52**: 568-573 [PMID: 12631671 DOI: 10.1136/gut.52.4.568]
- 37 **Mutch MG**. Laparoscopic colectomy in the elderly: when is too old? *Clin Colon Rectal Surg* 2006; **19**: 33-39 [PMID: 20011451 DOI: 10.1055/s-2006-939529]
- 38 **Biondi A**, Grosso G, Mistretta A, Marventano S, Toscano C, Drago F, Gangi S, Basile F. Laparoscopic vs. open approach for colorectal cancer: evolution over time of minimal invasive surgery. *BMC Surg* 2013; **13** Suppl 2: S12 [PMID: 24267544 DOI: 10.1186/1471-2482-13-S2-S12]
- 39 **Vara-Thorbeck C**, Garcia-Caballero M, Salvi M, Gutstein D, Toscano R, Gómez A, Vara-Thorbeck R. Indications and advantages of laparoscopy-assisted colon resection for carcinoma in elderly patients. *Surg Laparosc Endosc* 1994; **4**: 110-118 [PMID: 8180761]
- 40 **Hinoi T**, Kawaguchi Y, Hattori M, Okajima M, Ohdan H, Yamamoto S, Hasegawa H, Horie H, Murata K, Yamaguchi S, Sugihara K, Watanabe M. Laparoscopic versus open surgery for colorectal cancer in elderly patients: a multicenter matched case-control study. *Ann Surg Oncol* 2015; **22**: 2040-2050 [PMID: 25331007 DOI: 10.1245/s10434-014-4172-x]
- 41 **Kannan U**, Reddy VS, Mukerji AN, Parithivel VS, Shah AK, Gilchrist BF, Farkas DT. Laparoscopic vs open partial colectomy in elderly patients: Insights from the American College of Surgeons - National Surgical Quality Improvement Program database. *World J Gastroenterol* 2015; **21**: 12843-12850 [PMID: 26668508 DOI: 10.3748/wjg.v21.i45.12843]
- 42 **Vallribera Valls F**, Landi F, Espín Basany E, Sánchez García JL, Jiménez Gómez LM, Martí Gallostra M, Salgado Cruz L, Armengol Carrasco M. Laparoscopy-assisted versus open colectomy for treatment of colon cancer in the elderly: morbidity and mortality outcomes in 545 patients. *Surg Endosc* 2014; **28**: 3373-3378 [PMID: 24928231 DOI: 10.1007/s00464-014-3597-4]
- 43 **Delgado S**, Lacy AM, García Valdecasas JC, Balagué C, Pera M, Salvador L, Momblan D, Visa J. Could age be an indication for laparoscopic colectomy in colorectal cancer? *Surg Endosc* 2000; **14**: 22-26 [PMID: 10653230 DOI: 10.1007/s004649900004]
- 44 **Law WL**, Chu KW, Tung PH. Laparoscopic colorectal resection: a safe option for elderly patients. *J Am Coll Surg* 2002; **195**: 768-773 [PMID: 12495308 DOI: 10.1016/S1072-7515(02)01483-7]
- 45 **Vignali A**, Di Palo S, Tamburini A, Radaelli G, Orsenigo E, Staudacher C. Laparoscopic vs. open colectomies in octogenarians: a case-matched control study. *Dis Colon Rectum* 2005; **48**: 2070-2075 [PMID: 16086219 DOI: 10.1007/s10350-005-0147-0]
- 46 **Bardram L**, Funch-Jensen P, Kehlet H. Rapid rehabilitation in elderly patients after laparoscopic colonic resection. *Br J Surg* 2000; **87**: 1540-1545 [PMID: 11091243 DOI: 10.1046/j.1365-2168.2000.01559.x]
- 47 **O'Connell JB**, Maggard MA, Ko CY. Cancer-directed surgery for localized disease: decreased use in the elderly. *Ann Surg Oncol* 2004; **11**: 962-969 [PMID: 15525824 DOI: 10.1007/BF02524023]
- 48 **Finlayson E**, Zhao S, Varma MG. Outcomes after rectal cancer surgery in elderly nursing home residents. *Dis Colon Rectum* 2012; **55**: 1229-1235 [PMID: 23135580 DOI: 10.1097/DCR.0b013e318267bfe3]
- 49 **Bouvier AM**, Launoy G, Lepage C, Faivre J. Trends in the management and survival of digestive tract cancers among patients aged over 80 years. *Aliment Pharmacol Ther* 2005; **22**: 233-241 [PMID: 16091061 DOI: 10.1111/j.1365-2036.2005.02559.x]
- 50 **Heald RJ**, Moran BJ, Ryall RD, Sexton R, MacFarlane JK. Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978-1997. *Arch Surg* 1998; **133**: 894-899 [PMID: 9711965 DOI: 10.1001/archsurg.133.8.894]
- 51 **Kim HS**, Ko S, Oh NG. Long-term results of extended intersphincteric resection for very low rectal cancer: a retrospective study. *BMC Surg* 2016; **16**: 21 [PMID: 27090553 DOI: 10.1186/s12893-016-0133-6]
- 52 **Folkesson J**, Birgisson H, Pahlman L, Cedermark B, Glimelius B, Gunnarsson U. Swedish Rectal Cancer Trial: long lasting benefits from radiotherapy on survival and local recurrence rate. *J Clin Oncol* 2005; **23**: 5644-5650 [PMID: 16110023 DOI: 10.1200/JCO.2005.08.144]
- 53 **Basili G**, Lorenzetti L, Biondi G, Preziuso E, Angrisano C, Carneccchi P, Roberto E, Goletti O. Colorectal cancer in the elderly. Is there a role for safe and curative surgery? *ANZ J Surg* 2008; **78**: 466-470 [PMID: 18522567 DOI: 10.1111/j.1445-2197.2008.04536.x]
- 54 **Schiffmann L**, Ozcan S, Schwarz F, Lange J, Prall F, Klar E. Colorectal cancer in the elderly: surgical treatment and long-term survival. *Int J Colorectal Dis* 2008; **23**: 601-610 [PMID: 18343931 DOI: 10.1007/s00384-008-0457-5]
- 55 **Devon KM**, Vergara-Fernandez O, Victor JC, McLeod RS. Colorectal cancer surgery in elderly patients: presentation, treatment, and outcomes. *Dis Colon Rectum* 2009; **52**: 1272-1277 [PMID: 19571704 DOI: 10.1007/DCR.0b013e3181a74d2e]
- 56 **Paksoy M**, Ipek T, Colak T, Cebeci H. Influence of age on prognosis and management of patients with colorectal carcinoma. *Eur J Surg* 1999; **165**: 55-59 [PMID: 10069635 DOI: 10.1080/110241599750007513]

P- Reviewer: Kleeff J, Uggeri F, van Oudheusden TR

S- Editor: Qi Y **L- Editor:** A **E- Editor:** Li D





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

