JBUON 2017; 22(3): 686-691
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

Charlson comorbidity index for evaluation of the outcomes of elderly patients undergoing laparoscopic surgery for colon cancer

Yun Huang, Yuxing Zhang, Jianjun Li, Gang Liu
Department of General Surgery, Navy General Hospital, Beijing 100048, People's Republic of China

Summary

Purpose: *We investigated the effectiveness of the Charlson comorbidity index (CCI) for predicting postoperative 30-day complications and long-term survival outcomes of elderly patients who underwent laparoscopic surgery for colon cancer with radical intent.*

Methods: *We reviewed 178 patients aged ≥70 years who underwent laparoscopic surgery for colon cancer with radical intent between January 2008 and December 2015. Patients were divided into high CCI (CCI ≥ 3; n=71) and low CCI (CCI < 3; n=107) groups for comparative analyses of differences in their short- and long-term outcomes.*

Results: *Postoperative 30-day complications were more frequent in the high CCI group than in the low CCI group. Logistic regression analysis revealed that a high CCI was significantly predictive of postoperative 30-day complications. The 5-year overall survival (OS) rates were 65% and 54% for the low and high CCI groups, respectively (p=0.034) and their 5-year disease-free survival (DFS) rates were 60% and 47%, respectively (p=0.030).*

Conclusion: *CCI predicted the likelihood of postoperative 30-day complications and long-term survival outcomes of elderly patients who underwent laparoscopic surgery for colon cancer with radical intent.*

Key words: *Charlson comorbidity index, colectomy, colon cancer, elderly, laparoscopy, minimally invasive surgery*

Introduction

Increased life expectancy has led to a progressively aging population of patients with colon cancer [1-3]. Although some studies have identified clinicopathological and prognostic factors of elderly patients with colon cancer, their optimized care strategies remain controversial [4-6]. Surgery is a pivotal and common therapeutic option for elderly patients with operable colon cancer [7]. Moreover, laparoscopic surgery for colon cancer with radical intent is widely performed worldwide [8-12]. Some published randomized controlled trials have shown that laparoscopic surgery for colon cancer achieves better short-term surgical outcomes and similar long-term survival outcomes compared with open surgery [8-12]. Nevertheless, elderly patients with colon cancer sometimes experience serious postoperative complications and die because of colon cancer and/or concomitant disease relatively soon after undergoing surgery. To optimize the safety and quality of surgical methods, including laparoscopic surgery, for elderly patients with colon cancer, it is important to accurately predict the prognosis and risk of postoperative complications. Several scoring systems, such as the CCI and National Cancer Institute (NCI) Comorbidity Index, comprehensively evaluate the effects of patients' comorbidities [13-15]. CCI is the most widely used clinical scoring system to predict the survival of patients with malignancies [15]. Although some investigators

Correspondence to: Gang Liu, MD. Department of General Surgery, Navy General Hospital, Beijing 100048, People's Republic of China.
Tel and Fax: +86 10 66958371, E-mail: glbjcn@126.com
Received: 08/11/2016; Accepted: 19/11/2016

found that CCI is useful for predicting outcomes of patients with colon cancer [16-21], there are no reports of its reliability for predicting postoperative 30-day complications and long-term survival outcomes, particularly for elderly patients with colon cancer who undergo laparoscopic surgery.

Here, we conducted a retrospective study to investigate the utility of CCI for evaluating elderly patients with colon cancer who underwent laparoscopic surgery. For this purpose, we analyzed the correlation between their CCI scores and the prevalence of postoperative 30-day complications and evaluated their long-term survival outcomes.

Methods

We reviewed 178 consecutive patients with colon cancer aged ≥70 years and who underwent laparoscopic surgery for colon cancer with radical intent at our institution between January 2008 and January 2016. In general, candidates for laparoscopic surgery had clinical stage I–III disease. Patients with clinical T4 disease, N3 disease, and other malignant diseases were not candidates for laparoscopic surgery, and we excluded patients who underwent incomplete resection. Patients with disease that was initially classified according to earlier staging classifications, such as the 6th Edition of the TNM classification, were reevaluated according to the definitions of the 7th Edition [22-24]. Postoperative complications were defined as ≥ grade 2 for significant severe complications, according to the Clavien–Dindo classification system [25-29]. The technique of laparoscopic surgery with radical intent for colon cancer has been described elsewhere [11].

We defined the CCI items according to the literature [15]. Patients were scored using this CCI system and divided into high and low CCI groups with a cut-off score of 3 (low CCI group <3, n=107; high CCI group ≥3, n=71).

Follow-up data were collected from the outpatient follow-up database. Patients were examined in the outpatient department every 3 months for the first postoperative year, every 4-5 months for the next 2 years, and annually thereafter. The follow-up protocol was as follows: CEA every 3-4 months; CT of brain, chest, pelvis, and abdomen every 6 months; and annual endoscopic examination. If gastrointestinal symptoms were reported, an additional examination was conducted when necessary [30-35]. OS was calculated from the date of radical resection to the last follow-up visit or death from any cause. DFS was assessed from the date of radical resection until the date of cancer recurrence or death from any cause. Follow-up was terminated in October 2016. This study was approved by our institutional review board, although the need to obtain written informed consent from patients was waived because of its retrospective design.

Statistics

Categorical variables are presented as frequencies and percentages, and continuous variables are presented as median values with range. Statistical analyses were performed with the Chi-square test, Fisher's exact test, and Mann–Whitney *U* test for categorical and continuous variables, respectively. Univariate and multivariate analyses using a logistic regression model were performed to identify predicting factors of postoperative 30-day complications. Results are expressed as odds ratios (OD) with 95% confidence intervals (CI). OS and DFS rates were estimated by the Kaplan–Meier method, with differences in survival between groups compared by the log-rank test. The Cox proportional hazard model was used to identify significant predictive factors for patient survival outcomes. All analyses were performed using SPSS version 13 for Microsoft Windows version. $p<0.05$ was considered to be significant.

Results

Table 1 presents the clinicopathological characteristics of the patients and their surgical out-

Table 1. Clinicopathological characteristics of the two groups

Characteristics	*Low CCI group (n=107)*	*High CCI group (n=71)*	*p value*
Age, years, median (range)	72 (70-75)	75 (72-79)	0.020
Sex (Male: Female)	41:66	26:45	0.819
ASA score, n (%)			0.034
I	77 (72.0)	43 (60.6)	
II	23 (21.0)	11 (15.5)	
III	7 (6.5)	17 (23.9)	
BMI (kg/m^2), median (range)	21 (17-26)	20 (17-28)	0.125
Type of resection, n (%)			
Right hemicolectomy	48 (44.9)	29 (40.8)	0.597
Left hemicolectomy	38 (35.5)	28 (39.4)	0.596
Sigmoidectomy	21 (19.0)	14 (19.7)	0.988
Conversion, n (%)	11 (10.3)	8 (11.3)	0.835
Operative time, min, median (range)	190 (160-280)	170 (140-240)	0.251
Blood loss, ml, median (range)	140 (100-320)	160 (90-400)	0.108
Pathological stage (pTNM) (7th AJCC-UICC), n (%)			0.864
I	21 (19.6)	10 (14.1)	
II	47 (13.9)	37 (52.3)	
III	39 (36.4)	24 (33.8)	
Retrieved lymph nodes, median (range)	15 (12-23)	16 (13-20)	0.289
Residual tumor (R0/R1/R2)	107/0/0	71/0/0	1.000

CCI: Charlson Comorbidity Index

comes. There were significant differences between the two groups with respect to age (p=0.020), American Society of Anesthesiologists (ASA) score (p=0.034), and postoperative 30-day complications (p=0.008). Table 2 presents the postoperative 30-day complications of the two groups.

Table 2. Postoperative 30-day complications of the two groups

Complications	*Low CCI group (n=107)*	*High CCI group (n=71)*	*p value*
Postoperative 30-day complications, n (%)	11 (10.3)	18 (25.4)	0.008
Pneumonia, n (%)	2 (1.9)	7 (10.0)	0.042
Anastomotic leakage, n (%)	4 (3.7)	2 (2.8)	1.000
Intra-abdominal bleeding, n (%)	1 (0.9)	2 (2.8)	0.718
Intra-abdominal abscess, n (%)	2 (1.9)	2 (2.8)	1.000
Arrhythmia, n (%)	1 (0.9)	3 (4.2)	0.350
Acute coronary syndrome, n (%)	1 (0.9)	2 (2.8)	0.718

CCI: Charlson Comorbidity Index

The prevalence of postoperative 30-day complications, particularly for pneumonia (p=0.042), was significantly higher in the high CCI group. Table 3 presents the results of univariate and multivariate analyses of factors that predicted postoperative 30-day complications. Univariate analysis revealed that age, CCI, and ASA score were significant predictors of postoperative 30-day complications, and multivariate analysis identified only CCI as a significant predictor of postoperative 30-day complications (p=0.035; odds ratio 2.574; 95 % CI 1.258-3.584).

Table 4 presents the follow-up data for the two groups. During follow-up, the high and low CCI groups had similar disease recurrence rates, but the patients in the high CCI group were less likely to undergo treatment for cancer recurrence. The high CCI group had a high mortality rate, and more patients died of diseases unrelated to cancer compared with those in the low CCI group.

Table 4. Follow-up data of the two groups

Outcomes	*Low CCI group (n=107)*	*High CCI group (n=71)*	*p value*
Tumor recurrence, n (%)	25 (23.3)	19 (26.8)	0.607
Treat cancer recurrence with radical intent, n (%)	23 (21.5)	12 (16.9)	0.450
Mortality, n (%)	22 (20.6)	25 (35.2)	0.030
Died of cancer, n (%)	19 (17.8)	15 (21.1)	0.575
Died of non-cancer-related diseases	3 (2.8)	10 (19.1)	0.006

CCI: Charlson Comorbidity Index

The 5-year OS rates of the low and high CCI groups were 65% and 54%, respectively (p=0.034) (Figure 1). Table 5 presents the results of univariate and multivariate analyses of prognostic factors of OS. In univariate analysis, age, TNM stage, and CCI were significant prognostic factors of OS, and TNM stage and CCI were significant prognostic factors in the multivariate analysis.

The 5-year DFS rates of the low and high CCI groups were 60% and 47%, respectively (p=0.030) (Figure 2). Table 6 presents the results of univariate and multivariate analyses of prognostic factors of DFS. Univariate analysis identified age, TNM stage and CCI as significant prognostic factors of OS, and multivariate analysis identified only CCI as a significant prognostic factor.

Discussion

The incidence of colon cancer in older patients is expected to increase as the general population ages, particularly in countries such as China, Japan, and Korea. Although standard treatments for colon cancer are applicable to elderly patients, limited data are available for long-term outcomes of their treatments, making the development of evidence-based treatment recommendations challenging [36].

Table 3. Univariate and multivariate analyses of factors for postoperative 30-day complications

Factors	*Univariate favorable vs unfavorable*	*p value*	*OR*	*Multivariate 95% CI*	*p value*
Age	<75 vs ≥ 75 years	0.040	1.145	0.458-1.650	0.203
Sex	Male vs. Female	0.308	-	-	-
CCI	Low vs High CCI	0.008	2.574	1.258 – 3.584	0.035
Blood loss	<300 vs ≥300ml	0.102	-	-	-
Cancer stage	I-II vs ≥ III	0.098	-	-	-
ASA score	I-II vs ≥ III	0.031	1.236	0.652 – 1.801	0.096

CCI: Charlson Comorbidity Index, OR: odds ratio, 95% CI: 95% confidence interval

Table 5. Univariate and multivariate analyses for predictive factors of overall survival

Factors	*Univariate favorable vs unfavorable*	*p value*	*OR*	*Multivariate 95% CI*	*p value*
Age	<75 vs ≥ 75 years	0.043	1.230	0.505 – 1.658	0.090
Sex	Male vs female	0.369	-	-	-
CCI	Low vs High CCI	0.034	2.302	1.205 – 3.895	0.010
Blood loss	<300 vs ≥300ml	0.108	-	-	-
ASA score	I-II vs ≥ III	0.305	-	-	-
Cancer stage	I-II vs ≥ III	0.018	1.985	1.358 – 2.548	0.026

OR:odds ratio, 95% CI:95% confidence interval, CCI:Charlson Comorbidity Index

Table 6. Univariate and multivariate analyses for predictive factors of disease-free survival

Factors	*Univariate favorable vs unfavorable*	*p value*	*OR*	*Multivariate 95% CI*	*p value*
Age	<75 vs ≥ 75 years	0.015	1.205	0.789-1.962	0.092
Sex	Male vs female	0.129	-	-	-
CCI	Low vs high CCI	0.030	1.658	1.230-3.695	0.008
Blood loss	<300 vs ≥300ml	0.300	-	-	-
ASA score	I-II vs ≥ III	0.309	1.126	0.426-1.560	0.103
Cancer stage	I-II vs ≥ III	0.044	1.505	0.875-1.687	0.308

OR: odds ratio, 95% CI: 95% confidence interval, CCI: Charlson Comorbidity Index

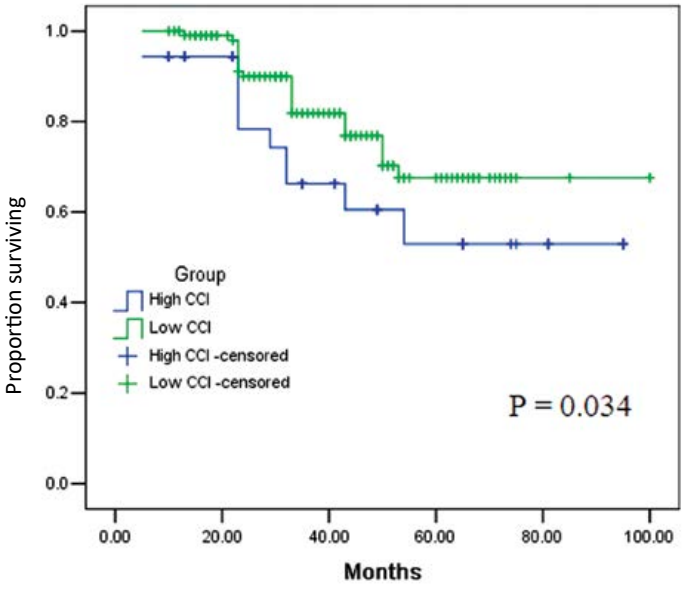

Figure 1. Kaplan-Meier overall survival of the two groups.

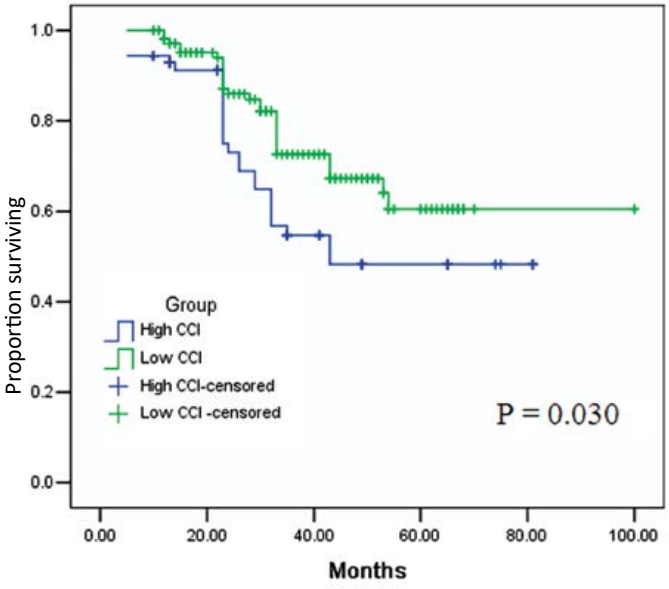

Figure 2. Kaplan-Meier disease-free survival of the two groups.

In the present study, we analyzed elderly patients who underwent laparoscopic surgery with radical intent. Laparoscopic surgery is an attractive option for elderly patients because of its low invasiveness. Patients who undergo laparoscopic surgery for colon cancer are hospitalized for shorter times and experience fewer postoperative complications compared with those who undergo open surgery [8-12]. Hinoi et al. performed a retrospective multicenter, matched case-control study of elderly patients who underwent laparoscopic surgery for colon cancer and found that the laparoscopic approach is associated with fewer complications as well as with shorter hospitalization compared with open surgery [37]. Moon et al. reported that a laparoscopic approach for colon cancer reduces postoperative morbidity in elderly patients and shortens hospitalization [38]. Therefore, laparoscopic surgery is likely the most appropriate approach for treating elderly patients with colon cancer in the future.

Many elderly patients with colon cancer have comorbidities; however, these patients represent a heterogeneous group, and their physiological status cannot be predicted simply according to age. Determining clinical scores using weighted comorbid conditions is useful for evaluating patients' physiological function and predicting postoperative morbidity and mortality. The most widely used scoring index is the validated CCI [13-15], which was used in several studies of cancer and in studies of elderly patients with cancer.

Several scoring systems, such as the Adult Comorbidity Evaluation-27 (ACE-27), National Institute on Aging (NIA), and NCI Comorbidity Index, were developed through the analysis of the literature [13-15]. Each system has advantages and disadvantages. For example, the comprehensive ACE-27 index accounts for disease severity when assessing the comorbidity burden. In contrast, the comprehensive NIA/NCI index does not consider disease severity. CCI is not as comprehensive compared with the others, although it weighs conditions according to the clinical significance. CCI is the most widely used among these scoring systems, according to the literature, and the CCI can be applied to most malignancies [13-15]. Here, CCI was a significant predictor of postoperative 30-day complications in elderly patients with colon cancer. For example, the total incidence of postoperative 30-day complications in the high CCI group was 25.4%, and the most common complication was pneumonia.

With some variations, patient outcomes in our study showed greater differences in OS between the low and high CCI groups compared with DFS, which reflects the higher mortality from diseases unrelated to cancer in the high CCI group. These findings indicate that close attention must be directed to cancer and other diseases. The high CCI group had lower OS and DFS, most likely because a high CCI score may hinder treatment for cancer recurrence, such as a second surgery, radiotherapy, or chemotherapy. Multivariate analyses revealed that CCI independently predicted postoperative complications and long-term survival outcomes in patients with colon cancer who underwent laparoscopic surgery.

This study has certain limitations. First, the study was retrospective, and the comorbidities were derived from medical records that varied in completeness. Second, the sample size was relatively small, and therefore, insufficient to reach definitive conclusions. Thus, the statistical power might have been insufficient, and a study of more subjects will be required to confirm these results.

Conclusion

CCI provided useful information about postoperative complications and the prognosis of elderly patients who underwent laparoscopic surgery for colon cancer with radical intent. Therefore, CCI may serve as an effective component of the pretreatment work.

Acknowledgements

We sincerely thank our hospital colleagues who participated in this research.

Conflict of interests

The authors declare no confict of interests.

References

1. Torre LA, Bray F, Siegel RL et al. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87-108.
2. Patricia Rios-Ibarra C, Janeth Rodriguez-Silva C, Alonso Lopez-Chukeny et al. Thymidylate synthase polymorphism in Mexican patients with colon cancer treated with 5-fluorouracil. JBUON 2016;21:935-940.
3. Demir S, Turan I, Aliyazicioglu Y. Selective cytotoxic effect of Rhododendron luteum extract on human colon and liver cancer cells. JBUON 2016;21:883-888.
4. Hu YL, Wang XB, Chen DD et al. Germanicol induces selective growth inhibitory effects in human colon HCT-116 and HT29 cancer cells through induction of apoptosis, cell cycle arrest and inhibition of cell migration. JBUON 2016;21:626-632.
5. Wu D, Li Q, Song G, Lu J. Identification of disrupted pathways in ulcerative colitis-related colorectal carcinoma by systematic tracking the dysregulated modules. JBUON 2016;21:366-374.

6. Vlad C, Kubelac P, Vlad D et al. Evaluation of clinical, morphopathological and therapeutic prognostic factors in rectal cancer. Experience of a tertiary oncology center. JBUON 2015;20:92-99.
7. 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;8:606-613.
8. Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004;350:2050-2059.
9. Fleshman J, Sargent DJ, Green E et al. Laparoscopic colectomy for cancer is not inferior to open surgery based on 5-year data from the COST Study Group trial. Ann Surg 2007;246:655-662; discussion 662-664.
10. Colon Cancer Laparoscopic or Open Resection Study Group; Buunen M, Veldkamp R, et al. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. Lancet Oncol 2009;10:44-52.
11. Jayne DG, Thorpe HC, Copeland J et al. Five-year follow-up of the Medical Research Council CLASICC trial of laparoscopically assisted versus open surgery for colorectal cancer. Br J Surg 2010;97:1638-1645.
12. Bagshaw PF, Allardyce RA, Frampton CM et al. Long-term outcomes of the australasian randomized clinical trial comparing laparoscopic and conventional open surgical treatments for colon cancer: the Australasian Laparoscopic Colon Cancer Study trial. Ann Surg 2012;256:915-919.
13. Sterling B, Cole R, Jen KK, Shieh JS. Surgical oncology in the elderly. Asian Pac J Surg Oncol 2015;1:83-100.
14. Zheng YF, Tan LK, Tan BH, Sterling H, Kane R. Principles of surgical oncology. Asian Pac J Surg Oncol 2015;1:17-26.
15. Chang CM, Yin WY, Wei CK et al. Adjusted Age-Adjusted Charlson Comorbidity Index Score as a Risk Measure of Perioperative Mortality before Cancer Surgery. PLoS One 2016;11:e0148076.
16. Krarup PM, Nordholm-Carstensen A, Jorgensen LN, Harling H. Association of Comorbidity with Anastomotic Leak, 30-day Mortality, and Length of Stay in Elective Surgery for Colonic Cancer: A Nationwide Cohort Study. Dis Colon Rectum 2015;58:668-676.
17. Caglar Bilgin B, Kahramanca S, Akin T et al. Factors influencing cost, length of hospital stay and mortality in colorectal cancer. JBUON 2015;20:1023-1029.
18. Siyar Ekinci A, Demirci U, Cakmak Oksuzoglu B et al. KRAS discordance between primary and metastatic tumor in patients with metastatic colorectal carcinoma. JBUON 2015;20:128-135.
19. Gunaldi M, Kocoglu H, Okuturlar Y et al. Heat shock protein 70 is a useful marker for predicting colorectal cancer. JBUON 2015;20:1464-1470.
20. Karabulut S,Usul Afsar C, Karabulut M et al. Clinical significance of serum interleukin-17 levels in colorectal cancer patients. JBUON 2016;21:1137-1145.
21. Zhan S, Wang X, Huang X, Zhu H. Magnetic resonance imaging in restaging rectal cancer after neoadjuvant chemoradiotherapy. J BUON 2015; 20:62-67.
22. Yung KW, Yung TT, Chung CY et al. Principles of cancer staging. Asian Pac J Surg Oncol 2015;1:1-16.
23. Horgan PG, Morrison DS, McMillan DC. Kondo H, Morita Y. Diagnostic workup of colon cancer. Asian Pac J Surg Oncol 2016;2:1-12.
24. Ahmed Farag AF, Elbarmelgi MY, Azim HA, Abozeid AA, Mashhour AN. TNMF versus TNM in staging of colorectal cancer. Int J Surg 2016;27:147-150.
25. Xiao H, Xie P, Zhou K et al. Clavien-Dindo classification and risk factors of gastrectomy-related complications: an analysis of 1049 patients. Int J Clin Exp Med 2015;8:8262-8268.
26. Dong J, Wang W, Yu K et al. Outcomes of laparoscopic surgery for rectal cancer in elderly patients. JBUON 2016;21:80-86.
27. Zaharie F, Ciorogar G, Zaharie R et al. Laparoscopic rectal resection versus conventional open approach for rectal cancer - a 4-year experience of a single center. JBUON 2015;20:1447-1455.
28. Guo C, Zhang Z, Ren B, Men X. Comparison of the long-term outcomes of patients who underwent laparoscopic versus open surgery for rectal cancer. JBUON 2015;20:1440-1446.
29. Clavien PA, Barkun J, de Oliveira ML et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187-196.
30. Wong CK, Guo VY, Chen J, Lam CL. Methodological and Reporting Quality of Comparative Studies Evaluating Health-Related Quality of Life of Colorectal Cancer Patients and Controls: A Systematic Review. Dis Colon Rectum 2016;59:1073-1086.
31. Raina K, Kumar S, Dhar D, Agarwal R. Silibinin and colorectal cancer chemoprevention: a comprehensive review on mechanisms and efficacy. J Biomed Res 2016;30.
32. Gao WD, Wu L, Sheng WZ. Surgical resection for colon cancer in the elderly. Asian Pac J Surg Oncol 2016;2:61-74.
33. Freeman HJ, Terracina KP. Radical surgery for colon cancer. Asian Pac J Surg Oncol 2016;2:13-24.
34. Sheng W, Zhang B, Chen W, Gu D, Gao W. Laparoscopic colectomy for transverse colon cancer: comparative analysis of short- and long-term outcomes. Int J Clin Exp Med 2015;8:16029-16035.
35. Cai K, Shen F, Cui JH, Yu Y, Pan HQ. Expression of miR-221 in colon cancer correlates with prognosis. Int J Clin Exp Med 2015;8:2794-2798.
36. Wang Y, Li P. Postoperative complications in elderly patients after colon cancer surgery. Asian Pac J Surg Oncol 2016;2:51-60.
37. Hinoi T, Kawaguchi Y, Hattori M et al. Laparoscopic versus open surgery for colorectal cancer in elderly patients: a multicenter matched case-control study. Ann Surg Oncol 2015;22:2040-2050.
38. Tei M, Wakasugi M, Kishi K, Tanemura M, Akamatsu H. Incidence and risk factors of postoperative delirium in elderly patients who underwent laparoscopic surgery for colorectal cancer. Int J Colorectal Dis 2016;31:67-73.