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ORIGINAL ARTICLE

Does Antiplatelet Therapy Affect Short-Term and Long-Term Outcomes of Patients Undergoing Surgery for Colorectal Cancer? - Surgical Radicality Versus Perioperative Antiplatelet-Related Morbidity Risks

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ABSTRACT

BACKGROUND: The effect of antiplatelet therapy(APT) on short-term and long-term outcomes in patients receiving surgery for colorectal cancer is still unknown.

METHODS: A total of 491 patients undergoing surgery for colorectal cancer between 2005 and 2011 were reviewed. The perioperative management protocol ("Kokura Protocol") included preoperative continuation of aspirin monotherapy and early postoperative reinstitution in patients at high thromboembolic risks. Both short-term and long-term outcomes of patients with APT (n = 148), including perioperative morbidity, disease free survival (DFS) and overall survival (OS), were compared to those of patients without APT (n = 343).

RESULTS: Among 148 patients with APT, none suffered from excessive hemorrhage intraoperatively. There were only 4 postoperative bleeding complications (0.8%) and 1 thromboembolic event (0.2%), and operative mortality was zero. In the APT and non-APT groups, 5-year DFS rates were 75.5% and 77.7% (P = 0.207), respectively; 5-year OS rates were 68.8% and 78.9% (P = 0.004), respectively. OS rates were lower in APT group compared with non-APT group, but multivariate analysis showed that APT was not a significant factor for either DFS or OS.

CONCLUSIONS: The resection of colorectal cancer in patients with APT was performed safely, and satisfactory long-term outcome was obtained without any decrease of surgical radicality. The Kokura Protocol is valid and feasible to secure both short-term and long-term outcomes of such patient population.

Key Words: Colorectal cancer; Colorectal surgery; Antiplatelet therapy; Bleeding complication; Thromboembolic complication; Disease-free survival; Overall survival; Risk factor

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INTRODUCTION

Antiplatelet therapy (APT) has an important role for primary and secondary prevention of cardiovascular and/or cerebrovascular complications[1,2]. Following the expansion of APT indication, increasing number of patients with APT are estimated to undergo a surgical procedure[3,4]. In patients with APT, perioperative risks of bleeding complications related to APT and thromboembolic complications associated with interruption of APT are major concerns[3-8]. We have shown that using perioperative antithrombotic management protocol ("Kokura Protocol"), both open and

laparoscopic abdominal surgery can be performed safely and satisfactorily in patients with APT[8,9]. However, the effect of APT on both short-term and long-term outcomes in patients receiving surgeries for malignancy still remains largely unknown.

The aim of this study is to review patients undergoing resection of colorectal cancer and to assess both short-term and long-term outcomes of surgery for colorectal cancer in patients who have been receiving APT.

METHODS

A total of 491 patients who had received radical resection of colorectal cancer in our institution between January 2005 and December 2011 were reviewed in this study. Patients diagnosed with Stage IV, or patients with insufficient information in the medical record were excluded from the study. Surgical procedures in this cohort included laparoscopic surgery (n = 191) and open surgery (n = 300). Lesion locations were colon (n = 318) and rectum (n = 173). Operations were performed according to Japanese guidelines and classification of colorectal cancer[10,11]. D2 lymphadenectomy was performed for Stage 0 and I cancer and D3 lymphadenectomy for Stage II and III cancer. If patients had poor general conditions or operations were in an emergent situation (e.g. bowel obstruction, cancer perforation, etc.), D1 lymphadenectomy was chosen. Laparoscopic surgery was generally performed for colon cancer without serosal invasion and rectal cancer in clinical Stage 0 and I. APT was not usually taken into account when we decided to choose the operative procedure, but open surgery was chosen when long time operation was not tolerable due to severe heart disease or decreased pulmonary function. All procedures were performed by or under the guidance of one of the attending surgeons at our institution.

We have established our own perioperative protocol ("Kokura Protocol") about antithrombotic agents and risk stratification using several guidelines concerning antithrombotics as references[8,9]. The perioperative management of antiplatelet agents is shown in Figure 1. In patients at low thromboembolic risk, APT was interrupted 1 week before surgery and reinstituted 1 or 2 days after surgery (protocol A). For patients at high thromboembolic risk, aspirin monotherapy was maintained preoperatively (protocol B). Emergent operations were performed without reversal of the antiplatelet effect. If patients received chronic oral anticoagulation (mainly warfarin) therapy, patients were managed by interruption of oral anticoagulation 5 to 7 days before surgery, bridging anticoagulation with unfractionated heparin, and early postoperative re-institution. High thromboembolic risk patients were defined as follows: (1) patients with drug-non-eluting coronary bear metal stent (BMS) implantation within two months; (2) patients with drug-eluting coronary stent (DES) implantation (regardless of the interval between DES implantation and surgical procedures); (3) patients who received cerebrovascular reconstruction within two months; (4) patients who had recent-onset cerebral infarction or transient ischemic attack; and (5) patients having cardiovascular or cerebrovascular diseases who were assessed as "high risk" for other reasons by cardiac/cerebral specialists.

Demographics, diagnosis, surgical treatments and postoperative outcomes were collected from the electronic surgery database as well as hospital and clinic charts. The status of patients' symptoms and functions about daily living abilities was described using the ECOG Scale of Performance Status (PS)[12]. Postoperative complications were assessed and categorized according to Clavien-Dindo classification (CDC)[13] and CDC class II and more was considered significant. Postoperative bleeding complications included intraluminal bleeding, intra-abdominal bleeding, and abdominal wall hematoma. Intraluminal bleeding was defined as gastrointestinal bleeding with a significant decline in hemoglobin and requiring red blood cell (RBC) transfusion and/or therapeutic intervention. Intra-abdominal bleeding was diagnosed by abdominal distention or bloody abdominal drainage accompanied by imaging studies and a drop in hemoglobin. Bleeding complications with CDC class II were defined as minor bleeding complications, whereas those with CDC class III or more were defined as major bleeding complications. Thromboembolic complications included cerebral infarction, myocardial infarction (either due to stent thrombosis or not), pulmonary thromboembolism, and mesenteric infarction, which was diagnosed clinically and confirmed by imaging studies. The status of cancer was described according to TNM classification of malignant tumors. Operative mortality included death within 30 days after surgery.

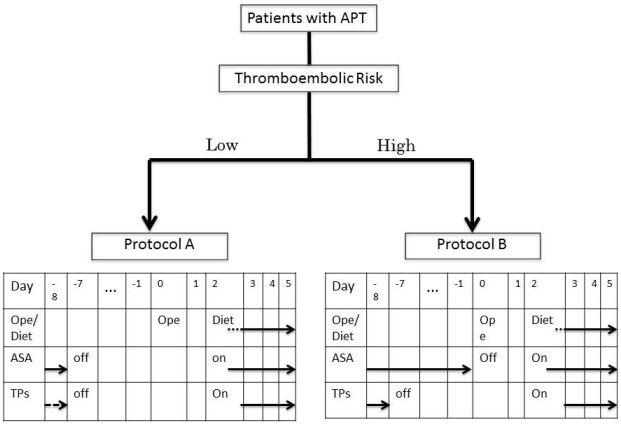

Figure 1 Our perioperative management protocol of patients receiving antiplatelet therapy (APT). The management generally consists of interruption of APT one week before surgery and early postoperative re-institution in low thromboembolic risk patients, whereas at least a single antiplatelet agent (usually aspirin) was maintained preoperatively in case of high thromboembolic risk or emergent situation. Abbreviations: APT: antiplatelet therapy, Ope: operation, ASA: acetylsalicylic acid (aspirin), TPs: thienopyridines.

The primary outcome included both disease free survival (DFS) and overall survival (OS). DFS was defined as the time from surgery to relapse or death without recurrence, whichever occurred first. The duration of follow-up was defined as the number of months from surgery until the last follow-up visit or data cutoff. OS was measured from surgery until death from any cause. Perioperative and outcome variables were compared between patients with APT (APT group, n = 148) and without APT (non-APT group, n = 343), and univariate and multivariate analysis were used to clarify the risk factors for DFS and OS.

The categorized date in each group was compared by chi-square or Fisher's exact probability test. Continuous variables in the characteristics were expressed as a median with range and compared by one-way ANOVA or Kruskal-Wallis test. Non-parametric variables were also compared using Kruskal-Wallis test with Scheffe's F test. Comparisons of DFS and OS between groups were performed using a two-sided stratified log-rank test. Hazard ratio (HR) with 95% confidence interval (CI) was calculated using COX proportional hazard models. Multivariate COX models began with all suspected prognostic variables obtained by univariate analysis. Survival curves were presented according to Kaplan-Meier methods. Statistical significance was set at $p < 0.05$. Data were analyzed using the SPSS package software.

This study was approved by our institutional review board.

RESULTS

Regular APT use was seen in 148 patients (30.1%) in this cohort. Table 1 shows profile of APT patients undergoing surgery for colorectal cancer. Concerning the type and agents of APT, single APT was dominant with the rate of 73.0% and aspirin was the most preferred agent. Angina pectoris (68.9%) and cerebral infarction (29.0%) explain the most of indications for APT. Among APT group, 18 patients (12.2%) required preoperative continuation of APT.

The patient characteristics for this cohort are listed in table 2 and table 3. A race of patients in the cohort was exclusively Asian and no other races were observed. Male gender ($P < 0.001$), patients with poor American Society of Anesthesiologists (ASA) score (ASA 3 or 4) ($P < 0.001$), diabetes mellitus ($P < 0.001$), history of cerebral infarction or transient ischemic attack ($P < 0.001$), maintenance of hemodialysis or peritoneal dialysis ($P < 0.001$), history of heart failure ($P < 0.001$), history of percutaneous coronary intervention (PCI) ($P < 0.001$), use of anticoagulation ($P<0.001$), and intraoperative RBC transfusion ($P = 0.006$) were more prevalent in the APT group, on the other hand non-APT group included more patients with laparoscopic surgery ($P = 0.021$) or perioperative chemotherapy ($P = 0.026$). There was no difference between the groups in the site of surgery (colon or rectum), the grade of lymphadenectomy (D1, D2 or D3) or cancer stage (0, I, II or III). There were only four postoperative bleeding complications (0.8%) and one thromboembolic event (0.2%) in a whole cohort.

Figure 2 shows the DFS and OS in the APT and non-APT groups. In the APT and non-APT groups, 5-year DFS rates were 75.5% and 77.7% ($P = 0.458$), respectively; median follow-up time was 31 months and 37 months, respectively. Five-year OS rates were 68.8% with 36 months of median follow-up in the APT group, as compared with 78.9% with 42 months of median follow-up in the non-APT group ($P = 0.004$).

Figure 3 shows the DFS and OS among patients in each cancer stage. Five-year DFS rates in the APT and non-APT groups were 89.2% and 95.7% among patients with Stage I disease, 80.3% and 77.2% among Stage II patients, and 61.9% and 63.6% among stage III patients. No significant difference was seen in each stage. Five-year OS in the APT and non-APT groups were 100% and 87.5% among patients with Stage 0 disease, 82.4% and 94.4% among patients with Stage I disease, 58.4% and 88.9% among patients with Stage II disease, and 69.4% and 63.2% among Stage III disease. The cause of death in each stage was shown in table 4. In the APT group death from other disease was more likely than in the non-APT group.

Univariate and multivariate analyses for DFS and OS were shown in table 5 and 6. In DFS, gender, cancer stage, intraoperative RBC transfusion, and perioperative chemotherapy were associated on univariate analysis, and using multivariate analysis, female gender ($P = 0.003$; HR = 2.099), cancer stage III ($P = 0.005$; HR = 2.141), and perioperative chemotherapy ($P = 0.005$; HR = 2.142) were significant prognostic factors. In OS, while PS, ASA score, maintenance of hemodialysis or peritoneal dialysis, history of heart failure, history of PCI, APT, cancer stage, intraoperative RBC transfusion, and perioperative chemotherapy were significant on univariate analysis, poor PS (grade 3 or 4) ($P = 0.001$; HR = 4.006), history of heart failure ($P = 0.006$; HR = 2.382), history of PCI ($P = 0.02$; HR = 2.562), cancer stage III ($P = 0.01$; HR = 2.088), and intraoperative RBC transfusion ($P = 0.005$; HR = 2.477) were independently associated with reduced OS. APT was not a significant factor for either DFS ($P = 0.207$; HR = 1.377) or OS ($P = 0.213$; HR = 0.605).

Table 1 Profile of antiplatelet therapy patients undergoing colorectal surgery.

Variable	*n* (%)
APT group, total	148 (100)
Type and agents used in APT	
Single APT	108 (73.0)
Multidrug APTs	40 (27.0)
Indication of APT	
Angina pectoris	102 (68.9)
s/p PCI with BMS	60 (40.5)
s/p PCI with DES	12 (8.1)
s/p CABG	18 (12.2)
Others	12 (8.1)
History of cerebral infarction	43 (29.1)
ICA stenosis	10 (6.8)
Others	12 (8.1)
Preoperative continuation of APT	
Yes	18 (12.2)
No	130 (87.8)

APT: antiplatelet therapy, PCI: percutaneous coronary intervention, BMS: bare metal stent, DES: drug-eluting stent, CABG: coronary artery bypass graft, ICA: internal carotid artery.

Table 2 Background characteristics of patients in the cohort.

Variables	APT (*n* = 148)	non-APT (*n* = 343)	Total (*n* = 491)	*p* value
Age median(range)	75 (55-96)	69 (41-94)	71 (41-96)	
Gender, *n*(%)				
Female	36 (24.3)	155 (45.2)	191	
Male	112 (75.7)	188 (54.8)	300	<0.001
BMI, n(%)				
<30kg/m^2	145 (98.0)	335 (97.7)	480	
⩾30 kg/m^2	3 (2.0)	8 (2.3)	11	1
Performance status, *n*(%)				
0-2	141 (95.3)	333 (97.1)	474	
3,4	7 (4.7)	10 (2.9)	17	0.419
ASA score, *n*(%)				
1,2	70 (47.3)	301 (87.8)	371	
3,4	78 (52.7)	42 (12.2)	120	<0.001
Diabetes mellitus, *n*(%)				
Yes	51 (34.5)	43 (12.5)	94	
No	97 (65.5)	300 (87.5)	397	<0.001
History of CI/TIA, *n*(%)				
Yes	45 (30.4)	10 (2.9)	55	
No	102 (68.9)	333 (97.1)	435	<0.001
Current Hemodialysis/PD, *n*(%)				
Yes	11 (7.4)	2 (0.6)	13	
No	137 (92.6)	341 (99.4)	478	<0.001
History of CHF, *n*(%)				
Yes	44 (29.7)	16 (4.7)	60	
No	104 (70.3)	327 (95.3)	431	<0.001
History of PCI, *n*(%)				
Yes	78 (52.7)	0 (0)	78	
No	70 (47.3)	343 (100)	413	<0.001
Anticoagulation used, *n*(%)				
Yes	23 (15.5)	18 (5.2)	41	
No	125 (84.5)	325 (94.8)	450	<0.001

APT: antiplatelet therapy, BMI: body mass index, ASA: American Society of Anesthesiologists, CI: cerebral infarction, TIA: transient ischemic attack, PD: peritoneal dialysis, CHF: congestive heart failure, PCI: percutaneous coronary intervention.

DISCUSSION

This retrospective cohort study showed that APT does not significantly affect either short-term or long-term outcomes of patients undergoing radical resection of colorectal cancer. There were only 4 postoperative bleeding complications (0.8%) and 1 thromboembolic event (0.2%), and operative mortality was zero in the whole cohort. Although 5-year OS rates in APT group appeared to be lower than those of non-APT group, statistical analysis suggested that the reduced OS rates largely resulted from severe underlying disease including heart failure or cardiovascular disease, and were not related to APT.

Table 3 Perioperative characteristics of patients in the cohort.

Variables	APT (n = 148)	non-APT (n = 343)	Total (n = 491)	p
Type of surgery, n(%)				
Colon	98 (66.2)	220 (64.1)	318	
Rectum	50 (33.8)	123 (35.9)	173	0.682
Laparoscopic surgery, n(%)				
Yes	46 (31.1)	145 (42.3)	191	
No	102 (68.9)	198 (57.7)	300	0.021
TNM Stage, n(%)				
0-II	94 (63.5)	228 (66.5)	322	
III	54 (36.5)	115 (33.5)	169	0.536
Grade of lymphadenectomy, n(%)				
D1	17 (11.5)	25 (7.3)	42	
D2	79 (53.4)	169 (49.3)	248	
D3	52 (35.1)	149 (43.4)	201	
Perioperative chemotherapy, n(%)				
Yes	29 (19.6)	101 (29.4)	130	
No	119 (80.4)	241 (70.3)	360	0.026
Estimeted blood loss, n(%)				
<1000 ml	147 (99.3)	337 (98.3)	484	
⩾1000 ml	1 (0.7)	6 (1.7)	7	0.68
Intraoperative RBC transfusion, n(%)				
Yes	20 (13.5)	19 (5.5)	39	
No	128 (86.5)	324 (94.5)	452	0.006
Bleeding complications, n(%)				
Yes	1 (0.7)	3 (0.9)	4	
No	147 (99.3)	340 (99.1)	487	1
Thromboembolic complications, n(%)				
Yes	1 (0.7)	0 (0)	1	
No	147 (99.3)	343 (100)	490	0.301

APT: antiplatelet therapy, RBC: red blood cell.

Table 5 Univariate analysis for DFS and OS.

Variables	Number	DFS events	p	DFS events	p
age					
<75yo	312	53 (17.0)	0.624	42 (13.5)	0.093
>=75yo	179	34 (19.0)		35 (19.6)	
Gender					
Female	191	45 (23.6)	0.008	35 (18.3)	0.205
Male	300	42 (14.0)		42 (14)	
Performance status					
0-2	474	87 (18.4)	0.053	69 (14.6)	0.002
3,4	17	0 (0)		8 (47.1)	
ASA score					
1,2	371	63 (17.0)	0.492	49 (13.2)	0.013
3,4	120	24 (20.0)		28 (23.3)	
Diabetes mellitus					
Yes	94	14 (14.9)	0.548	14 (14.9)	0.876
No	397	73 (18.4)		63 (15.9)	
History of CI/TIA					
Yes	55	11 (20.0)	0.708	8 (14.5)	1
No	435	76 (17.5)		69 (15.9)	
Current Hemodialysis/PD					
Yes	13	1 (7.69)	0.481	5 (38.5)	0.038
No	478	86 (18.0)		72 (15.1)	
History of CHF					
Yes	60	13 (21.7)	0.372	20 (33.3)	<0.001
No	431	74 (17.2)		57 (13.2)	
History of PCI					
Yes	78	17 (21.8)	0.332	23 (29.5)	0.001
No	413	70 (16.9)		54 (13.1)	
Anticoagulation used					
Yes	41	7 (17.1)	1	7 (17.1)	0.822
No	450	80 (17.7)		70 (15.6)	
APT used					
Yes	148	27 (18.2)	0.898	32 (21.6)	0.021
No	343	60 (17.5)		45 (13.1)	
Cancer Stage					
0-II	322	34 (10.6)	<0.001	35 (10.9)	<0.001
III	169	53 (31.4)		42 (24.9)	
Estimated blood loss					
<1000ml	484	84 (17.4)	0.11	75 (15.5)	0.302
>=1000ml	7	3 (42.9)		2 (28.6)	
Intraoperative RBC transfusion					
Yes	39	13 (33.3)	0.014	13 (33.3)	0.004
No	452	74 (16.4)		64 (14.2)	
Perioperative chemotherapy					
Yes	130	47 (36.2)	<0.001	29 (22.3)	0.024
No	360	40 (11.1)		48 (13.3)	

DFS: disease free survival, OS: overall survival, ASA: American Society of Anesthesiologists, CI: cerebral infarction, TIA: transient ischemic attack, PD: peritoneal dialysis, CHF: congestive heart failure, PCI: percutaneous coronary intervention, APT: antiplatelet therapy, RBC: red blood cell.

Table 4 Cause of death in the cohort.

	APT (n=148)			non-APT (n=343)		
	n	Death from colorectal cancer	Death from other disease	n	Death from colorectal cancer	Death from other disease
Stage 0	5	0 (0%)	0 (0%)	8	0 (0%)	1 (12.5%)
Stage I	33	2 (6.1%)	2 (6.1%)	85	0 (0%)	3 (3.5%)
Stage II	56	3 (5.4%)	12 (21.4%)	135	9 (6.7%)	3 (2.2%)
Stage III	54	8 (14.8%)	5 (9.3%)	115	20 (17.4%)	9 (7.8%)

Table 6 Multivariate analysis for DFS and OS.

Variables	P value	Hazard Ratio	95% CI	P value	Hazard Ratio	95% CI
Female gender	0.003	2.099	1.342 to 3.283	-	-	
Performance status ⩾ 3	-	-	-	0.001	4.006	1.772 to 9.054
ASA score ⩾ 3	-	-	-	0.605	1.171	0.643 to 2.133
Current Hemodialysis/PD	-	-	-	0.057	2.773	0.971 to 7.923
History of CHF	-	-	-	0.006	2.382	1.282 to 4.428
History of PCI	-	-	-	0.02	2.562	1.163 to 5.644
Cancer Stage III	0.005	2.141	1.253 to 3.663	0.01	2.088	1.195 to 3.650
Intraop RBC transfusion	0.003	2.499	1.366 to 4.571	0.005	2.477	1.308 to 4.693
Periop chemotherapy	0.005	2.142	1.260 to 3.642	0.867	0.951	0.527 to 1.714
APT	0.207	1.377	0.838 to 2.262	0.213	0.605	0.275 to 1.333

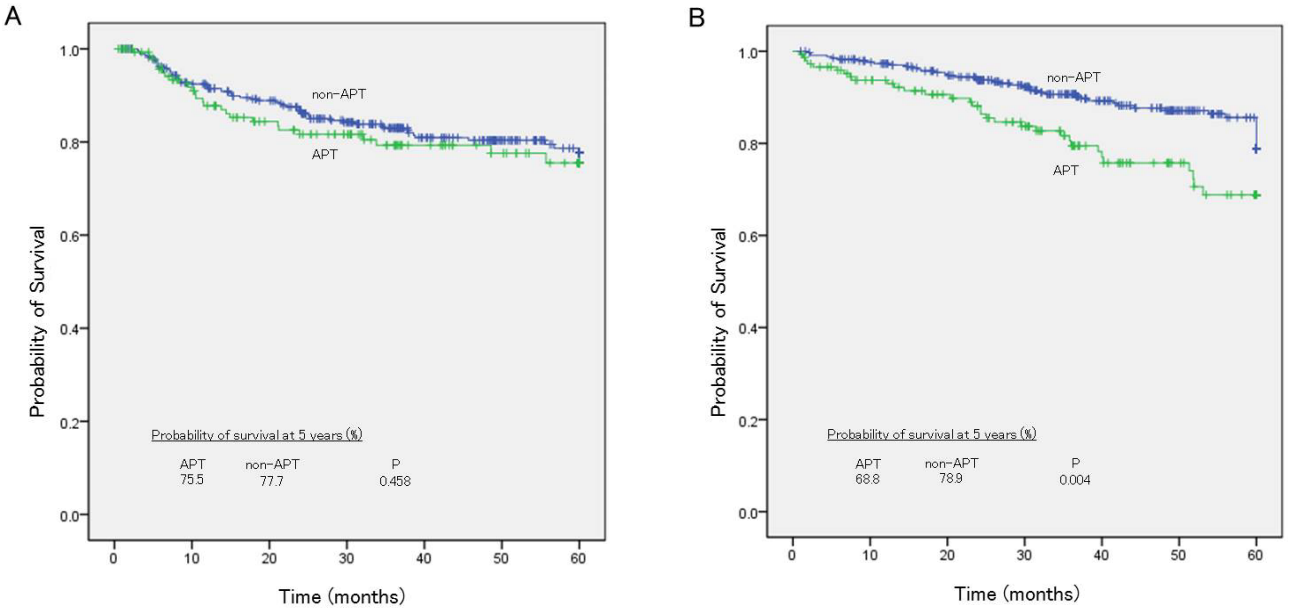

Figure 2 Kaplan-Meier estimates of disease free survival (DFS) and overall survival (OS) by antiplatelet therapy. (A) There was no significant difference in 5-year DFS rates between APT and non-APT groups (75.5% *vs*. 78.9%, $p = 0.458$). (B) Five-year OS rates were lower in APT group compared with non-APT group (68.8% *vs*. 78.9%, $p = 0.004$).

With the widespread use of antiplatelet agents for secondary prevention following coronary stent implantation, bypass surgery, non-cardiogenic ischemic stroke or TIA[1,14,15], it is not uncommon that patients with APT undergo a surgical procedure. Approximately 5% to 15% of patients receiving coronary stent implantation are estimated to undergo a surgical procedure within 2 years[4]. Berger PB, *et al*[3] reported more than 4% of patients required a major non-cardiac surgery in the year after placement of DES.

Bleeding and thromboembolic complications are major perioperative concerns in patients with APT. Interruption of APT may cause thromboembolic events, whereas continuation of antiplatelet agents is associated with an increased risk of bleeding[16,17]. Some clinical studies have shown no increase in the risk of perioperative bleeding 5-7 days following the withdrawal of antiplatelet agents[18-20]. Therefore, if the risk of thromboembolism is low, interruption of APT one week before surgery should be adequate. However, if the thromboembolic risk is high, perioperative continuation of APT should be considered. Particularly in patients with coronary stent, continuation of dual antiplatelet therapy (DAPT) with both aspirin and clopidogrel for at least 1 month after BMS implantation, and for at least 6 months after DES implantation is recommended[1]. Premature discontinuation of antiplatelet agents is one of risk factors of late stent thrombosis, which is uncommon but life-threatening complication with the mortality rate of between 9% and 45%[1,4,6].

Dealing with such conflicting problems is challenging. Following the expansion of APT indication, the question of their influence on long-term outcomes of surgery is raised. Is not the surgical radicality limited in order to avoid perioperative complications? Due to the limitation of study evidence, however, the effect of APT on surgical outcome in patients receiving surgery for malignancy still remains largely unknown. Some recent reports showed favorable short-term outcomes of surgical procedures on patients with APT[8,9,21-26]. Nevertheless, there are no specific reports relating to the effect of APT on both short-term and long-term outcome after surgery for malignancy. We have previously demonstrated that using a perioperative antithrombotic management protocol ("Kokura Protocol"), both open and laparoscopic abdominal surgery can be performed safely and satisfactorily in patients with APT[8,9]. In addition, the current study also showed that the Kokura Protocol is valid and feasible even in the setting of colorectal cancer surgery, resulting in neither increased perioperative complications nor decreased DFS/OS of colorectal cancer patients receiving APT.

Interestingly the HR for OS showed a low value of 0.6 (95% CI, 0.275 to 1.333), which suggests that APT was rather a potential improving factor of OS, although it was not significant. It might be because APT was effective for severe underlying disease and prevented death from cardiovascular and/or cerebrovascular events. It has been known that regular aspirin use reduces the risk of fatal colon cancer[27]. Randomized trials designed to assess the cardiovascular benefits of aspirin demonstrated that allocation to aspirin reduced the risk of cancer metastasis including colorectal cancer[28], and recent cohort study showed aspirin use after colon cancer diagnosis was associated with improved survival if tumors expressed HLA class I antigen[29]. Although our data showed no significant difference in recurrence rates, aspirin may reduce the risk of colorectal cancer recurrence and extend OS.

This study has some limitations. It is a retrospective review from a single center, which lessens the efficacy of the statistical analysis and conclusion. This limitation will be mitigated in a later follow-up study or in a multi-institutional, prospective study. Furthermore, it is uncertain if our perioperative management can be applied to Western populations. Despite these limitations, the current study provides important evidence about management of high thromboembolic risk patients undergoing colorectal cancer surgery.

CONCLUSION

This is the first study to examine the effects of APT on both short-term and long-term outcomes in patients undergoing surgery for colorectal cancer. Under rigorous Kokura Protocol including single APT continuation in high thromboembolic patients, operations were performed safely and satisfactory long-term outcome was achieved without any decrease of surgical radicality even for patients with APT.

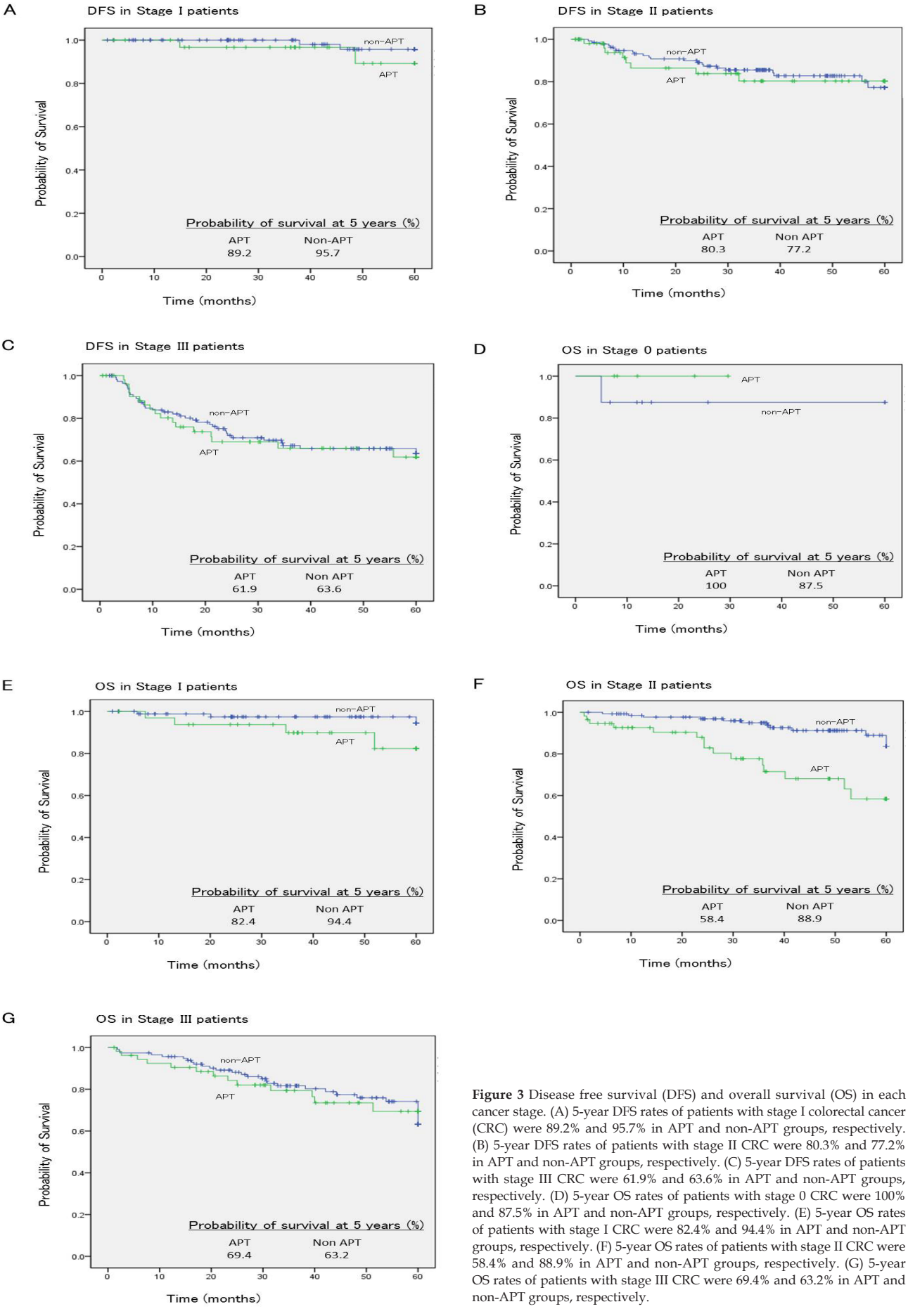

Figure 3 Disease free survival (DFS) and overall survival (OS) in each cancer stage. (A) 5-year DFS rates of patients with stage I colorectal cancer (CRC) were 89.2% and 95.7% in APT and non-APT groups, respectively. (B) 5-year DFS rates of patients with stage II CRC were 80.3% and 77.2% in APT and non-APT groups, respectively. (C) 5-year DFS rates of patients with stage III CRC were 61.9% and 63.6% in APT and non-APT groups, respectively. (D) 5-year OS rates of patients with stage 0 CRC were 100% and 87.5% in APT and non-APT groups, respectively. (E) 5-year OS rates of patients with stage I CRC were 82.4% and 94.4% in APT and non-APT groups, respectively. (F) 5-year OS rates of patients with stage II CRC were 58.4% and 88.9% in APT and non-APT groups, respectively. (G) 5-year OS rates of patients with stage III CRC were 69.4% and 63.2% in APT and non-APT groups, respectively.

CONFLICT OF INTERESTS

The authors declare that they do not have conflict of interests.

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