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Response to Reviewer's Comments

Reviewer's code: 03473233

I read with interest the manuscript by Moon at Al. The Authors retrospectively reviewed the data of patients who underwent colonoscopy at a single Endoscopy Unit and retrieved data about various obesity indices, as well as specific data about the exams. They found that female gender, a lower or higher BMI and a low VAT volume (in women) were associated with a prolonged cecal insertion time. Here are my concerns.

Major

1. Even if I am not an expert of obesity indexes, I found convincing the explanation why VAT may be associated with BMI in men (who have more abdominal and visceral fat) but less in women (whose fat is mainly in the femoral and gluteal regions). It would be great if the Authors analysed this association in the study population. If they confirmed such association, then it would be plausible that, while in women BMI and VAT are not related each other and they both show an association with CIT, in men BMI could 'absorb' the association between VAT and CIT. This should be checked (for instance by comparing the OR between VAT and CIT in a multivariate analysis with and without BMI) and discussed.

→ **We reanalyzed multivariate analysis considering VAT and BMI separately in total cohorts. BMI and VAT show an association with prolonged CIT. BMI < 23 kg/m^2 (OR, 1.84; 95% CI, 1.35-2.50; p<0.001), BMI ≥25 kg/m^2 (OR, 1.83; 95% CI, 1.34-2.50; p<0.001), VAT <500 cm^3 (OR, 1.57; 95% CI, 1.18-2.09; p=0.002) or VAT ≥1500 cm^3 (OR, 1.45; 95% CI, 1.00-2.09; p=0.047) shows an association with prolonged CIT.**

Table. Multivariate logistic regression analysis of predictors of prolonged CIT when BMI and VAT volume were considered separately

	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Gender									
Male	Ref			Ref			Ref		
Female	1.29	1.00-1.67	0.047	1.36	1.06-1.73	0.014	1.30	1.02-1.67	0.037
BMI (kg/m^2)									
< 23	1.62	1.16-2.25	0.004	1.84	1.35-2.50	<0.001			
23~24.9	Ref			Ref					
≥25	1.80	1.31-2.49	< 0.001	1.83	1.34-2.50	<0.001			
VAT volume (cm^3)									

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< 500	1.50	1.09-2.07	0.013				1.57	1.18-2.09	0.002
500~1499	Ref						Ref		
≥1500	1.27	0.86-1.88	0.223				1.45	1.00-2.09	0.047
Experience									
Attending physic	Ref			Ref			Ref		
Fellow	1.73	1.38-2.19	<0.001	1.73	1.37-2.17	<0.001	1.72	1.37-2.17	<0.001

→ **We reanalyzed multivariate analysis for comparing the OR between VAT and CIT with and without BMI for gender.**

In men, when considering VAT and BMI separately, only BMI shows an association with CIT. BMI < 23 kg/m^2 (OR, 1.69; 95% CI, 1.10-2.60; p = 0.017) or ≥ 25 kg/m^2 (OR, 1.88; 95% CI, 1.28-2.75; p = 0.001) shows an association with prolonged CIT.

In women, when considering VAT and BMI separately, BMI and VAT show an association with prolonged CIT. BMI <23 kg/m^2 (OR, 1.96; 95% CI, 1.25-3.10; p = 0.004) or VAT <500 cm^3 (OR, 1.66; 95% CI, 1.17-2.35; p = 0.005) shows an association with prolonged CIT.

As your opinion, these results imply that in women BMI and VAT are not related each other and they both show an association with CIT, while in men BMI could absorb the association between VAT and CIT.

Table. Predictive parameters of prolonged CIT according to gender by multivariate logistic regression analysis when BMI and VAT volume were considered simultaneously or separately

		OR	95% CI	p-valu	OR	95% CI	p-value	OR	95% CI	p-value
Male	BMI (kg/m^2)									
	< 23	1.58	1.00-2.50	0.049	1.69	1.10-2.60	0.017			
	23~24.9	Ref			Ref					
	≥25	1.82	1.22-2.71	0.003	1.88	1.28-2.75	0.001			
	VAT volume (cm^3)									
	< 500	1.40	0.80-2.43	0.236				1.41	0.86-2.33	0.178
	500~1499	Ref						Ref		
	≥1500	1.24	0.81-1.90	0.323				1.42	0.96-2.12	0.082
	Experience									
	Attending physic	Ref			Ref			Ref		

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	Fellow	1.93	1.41-2.63	<0.001	1.92	1.41-2.63	<0.001	1.88	1.38-2.57	<0.001
Female	BMI (kg/m^2)									
	< 23	1.66	1.02-2.69	0.041	1.96	1.25-3.10	0.004			
	23~24.9	Ref			Ref					
	≥25	1.79	1.02-3.13	0.042	1.71	0.99-2.96	0.053			
	VAT volume (cm^3)									
	< 500	1.54	1.03-2.31	0.034				1.66	1.17-2.35	0.005
	500~1499	Ref						Ref		
	≥1500	1.31	0.47-3.64	0.606				1.47	0.55-3.96	0.446
	Experience									
	Attending physic	Ref			Ref			Ref		
	Fellow	1.53	1.08-2.16	0.016	1.52	1.08-2.14	0.016	1.54	1.10-2.17	0.013

We added these results in RESULT and DISCUSSION section of the main manuscript and Supplement table 2.

Table 4 was revised to reflect these results.

Added in page 8, line 21

When BMI and VAT volume were considered separately by multivariate analysis in total cohort (Supplement table 2), being female, BMI less than 23 kg/m^2 (OR = 1.84; 95% CI, 1.35-2.50; p < 0.001) or greater than or equal to 25 kg/m^2 (OR = 1.83; 95% CI, 1.34-2.50; p < 0.001), VAT volume smaller than 500 cm^3 (OR, 1.57; 95% CI, 1.18-2.09; p = 0.002) or greater than or equal to 1500 cm^3 (OR, 1.45; 95% CI, 1.00-2.09; p = 0.047) and fellow involvement were independently associated with prolonged CIT.

Added in page 11, line 1

In our study, while in women BMI and VAT volume both showed an association with CIT, in men BMI could absorb the association between VAT volume and CIT.

Added Table (in page 29)

Supplement table 2. Predictive parameters of prolonged cecal insertion time by multivariate logistic regression analysis when BMI and VAT volume were considered separately

	OR	95% CI	p-value	OR	95% CI	p-value
Gender						
Male	Ref			Ref		

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Female	1.36	1.06-1.73	0.014	1.30	1.02-1.67	0.037
BMI (kg/m^2)						
< 23	1.84	1.35-2.50	<0.001			
23~24.9	Ref					
≥25	1.83	1.34-2.50	<0.001			
VAT volume (cm^3)						
< 500				1.57	1.18-2.09	0.002
500~1499				Ref		
≥1500				1.45	1.00-2.09	0.047
Experience						
Attending physicians	Ref			Ref		
Fellow	1.73	1.37-2.17	<0.001	1.72	1.37-2.17	<0.001

BMI = body mass index; VAT = visceral adipose tissue; OR = odds ratio; CI = confidence interval

Added in page 9, line 13

When BMI and VAT volume were considered separately by multivariate analysis for gender, in men, BMI less than 23 kg/m^2 (OR = 1.69; 95% CI, 1.10-2.60; p = 0.017) or greater than or equal to 25 kg/m^2 (OR = 1.88; 95% CI, 1.28-2.75; p = 0.001) and fellow involvement were independently associated with prolonged CIT. VAT volume, however, was not associated with prolonged CIT. In women, BMI less than 23 kg/m^2 (OR, 1.96; 95% CI, 1.25-3.10; p = 0.004), VAT volume smaller than 500 cm^3 (OR, 1.66; 95% CI, 1.17-2.35; p = 0.005) and fellow involvement were independently associated with prolonged CIT. BMI greater than or equal to 25 kg/m2 (OR = 1.71; 95% CI, 0.99-2.96; p = 0.053) was marginally associated with prolonged CIT.

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Revised Table (in page 20)

Table 4. Predictive parameters of prolonged cecal insertion time according to gender by multivariate logistic regression analysis when BMI and VAT volume were considered simultaneously or separately

		OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Male	BMI (kg/m^2)									
	< 23	1.58	1.00-2.50	0.049	1.69	1.10-2.60	0.017			
	23~24.9	Ref			Ref					
	≥25	1.82	1.22-2.71	0.003	1.88	1.28-2.75	0.001			
	VAT volume (cm^3)									
	< 500	1.40	0.80-2.43	0.236				1.41	0.86-2.33	0.178
	500~1499	Ref						Ref		
	≥1500	1.24	0.81-1.90	0.323				1.42	0.96-2.12	0.082
	Experience									
	Attending physicians	Ref			Ref			Ref		
	Fellow	1.93	1.41-2.63	<0.001	1.92	1.41-2.63	<0.001	1.88	1.38-2.57	<0.001
Female	BMI (kg/m^2)									

< 23	1.66	1.02-2.69	0.041	1.96	1.25-3.10	0.004			
23~24.9	Ref			Ref					
≥25	1.79	1.02-3.13	0.042	1.71	0.99-2.96	0.053			
VAT volume (cm^3)									
< 500	1.54	1.03-2.31	0.034				1.66	1.17-2.35	0.005
500~1499	Ref						Ref		
≥1500	1.31	0.47-3.64	0.606				1.47	0.55-3.96	0.446
Experience									
Attending physicians	Ref			Ref			Ref		
Fellow	1.53	1.08-2.16	0.016	1.52	1.08-2.14	0.016	1.54	1.10-2.17	0.013

BMI = body mass index; VAT = visceral adipose tissue; OR = odds ratio; CI = confidence interval

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2. BMI: the Authors put together patients who are overweight and obese (BMI>30). Did they check if these two subgroups are differently associated with CIT? I suggest to report this analysis – at least with a brief sentence in the text.

→ **Following your suggestion, we reanalyzed the association with CIT and BMI. BMI divided into four categories; BMI < 23 kg/m^2, 23-24.9 kg/m^2, 25-29.9 kg/m^2 and ≥30 kg/m^2. BMI was associated with a prolonged CIT in univariate analysis (p < 0.001).**

BMI < 23 kg/m^2 (OR, 1.62; 95% CI, 1.16-2.25; p = 0.004) or 25~29.9 kg/m^2 (OR, 1.81; 95% CI, 1.30-2.50; p < 0.001) were associated with prolonged CIT in multivariate analysis. However, BMI ≥ 30 kg/m^2 (OR, 1.79; 95% CI, 0.85-3.76; p = 0.126) was not associated with prolonged CIT in multivariate analysis. When considering VAT and BMI separately, BMI < 23 kg/m^2 (OR, 1.84; 95% CI, 1.32-2.50; p < 0.001) or 25~29.9 kg/m^2 (OR, 1.82; 95% CI, 1.32-2.50; p < 0.001) were associated with prolonged CIT in multivariate analysis. However, BMI ≥ 30 kg/m^2 (OR, 1.97; 95% CI, 0.97-4.02; p = 0.062) was not associated with prolonged CIT in multivariate analysis. Even though high BMI (≥ 30 kg/m^2) was not significant association in univariate and multivariate analysis, there was a trend of association with prolonged CIT. The cause of these result might be the low number of high BMI (n=45).

Table. Predictive parameters of prolonged CIT according to gender by multivariate logistic regression analysis when BMI (four categories) and VAT volume were considered simultaneously or separately

	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Gender									
Male	Ref			Ref			Ref		
Female	1.29	1.00-1.67	0.047	1.36	1.06-1.73	0.014	1.30	1.02-1.67	0.037
BMI (kg/m^2)									
< 23	1.62	1.16-2.25	0.004	1.84	1.32-2.50	<0.001			
23~24.9	Ref			Ref					
25~29.9	1.81	1.30-2.50	<0.001	1.82	1.32-2.50	<0.001			
≥30	1.79	0.85-3.76	0.126	1.97	0.97-4.02	0.062			
VAT volume (cm^3)									
< 500	1.50	1.09-2.07	0.013				1.57	1.18-2.09	0.002
500~1499	Ref						Ref		
≥1500	1.27	0.86-1.89	0.231				1.45	1.00-2.09	0.047
Experience									
Attending physic	Ref			Ref			Ref		

Fellow	1.73	1.38-2.19	<0.001	1.73	1.37-2.17	<0.001	1.72	1.37-2.17	<0.001

We added these results in the DISCUSSION section of the main manuscript.

Added in page 10, line 20

In our study, when higher BMI (≥ 25 kg/m^2) group was divided into overweight (25-29.9 kg/m^2) and obese (⩾ 30 kg/m^2) group, not obese group but overweight group was associated with prolonged CIT in multivariate analysis. Even though high BMI (⩾ 30 kg/m2) was not significant association in univariate and multivariate analysis, there was a trend of association with prolonged CIT. The cause of these result might be the low number of high BMI (n=45) (data not shown).

3. Discussion – paragraph starting with "In previous studies, poor bowel…". The Authors cite a 'marginally' association between poor bowel preparation and prolonged CIT in the fellow group at univariate analysis. Please report the evidence produced at multivariate analysis instead of univariate analysis and discuss accordingly.

→ **In subgroup analysis by experience of the colonoscopist, poor bowel preparation was marginally associated with prolonged CIT in the fellow group but not in the attending physician group in univariate analysis (p=0.050). In addition, poor bowel preparation was marginally associated with prolonged CIT in the fellow group in multivariate analysis (p = 0.056)**

The manuscript and Supplemental table 1 were revised accordingly.

Revised in page 12, line 15

In subgroup analysis by experience of the colonoscopist, poor bowel preparation was marginally associated with prolonged CIT in the fellow group but not in the attending physician group in multivariate analysis (p = 0.056, Supplement table 1).

Revised Table (in page 27)

Supplement table 1. Cecal insertion time according to study variables, by experience of the endoscopist, with Odd Ratios estimated by multivariate logistic regression analysis

		OR	95% CI	p -value
Attending Physician	Gender			
	Male	Ref		
	Female	1.42	1.01-2.00	0.043
	BMI (kg/m^2)			
	< 23	1.79	1.15-2.79	0.010

	23~24.9	Ref		
	⩾25	1.68	1.07-2.64	0.024
	VAT volume (cm^3)			
	< 500	1.29	0.84-1.98	0.240
	500~1499	Ref		
	⩾1500	1.23	0.73-2.07	0.435
Fellow	Age (years)			
	< 65	Ref		
	≥65	2.06	1.12-3.78	0.020
	BMI (kg/m^2)			
	< 23	1.36	0.81-2.27	0.240
	23~24.9	Ref		
	≥25	1.93	1.20-3.11	0.006
	WHR			
	Normal	Ref		
	High	0.69	0.41-1.17	0.170
	VAT (cm^3)			
	< 500	1.70	1.01-2.85	0.045
	500~1499	Ref		
	≥1500	1.22	0.67-2.21	0.511
	Bowel preparation			
	Excellent to fair	Ref		
	Poor to inadequate	1.53	0.99-2.35	0.056

OR = odd ratios; CI = confidence interval; BMI = body mass index; VAT = visceral adipose tissue; WHR = waist-to-hip circumference ratio

4. Conclusion. The Authors suggest that the results of their study could be useful 'for patient

selection and increasing the completion rate of colonoscopy'. I don't agree with this conclusion. First, the outcome of the analysis is CIT, not completion rate. Moreover, as far as can be deduced from the reported data, colonoscopy was incomplete only in 9 patients out of 1717 (Figure 1). Second, as the measurement of VAT requires abdominal CT, are the Authors really suggesting that patients could undergo such exam in order to identify those who will potentially need a prolonged time for cecal intubation? My personal conviction is that the association between VAT and CIT is not strong enough to gain an operative significance. Nevertheless, I suggest to develop conclusions with some more specific hints about the possible utilisation of obesity indexes, that are the specific focus of the paper.

→ **Following your suggestion, we revised conclusion.**

Revised in page 13, line 3

Prediction of potentially difficult patient may help the colonoscopist decide on scheduling, sedation and vital monitoring requirements, and the need for better colonoscopic expertise. Being female, lower or higher BMI than the normal range, low VAT volume and fellow involvement were predictors of longer CIT. Among obesity indices, lower or higher BMI than the normal range and low VAT volume were associated with longer CIT. Our findings suggest a role of VAT volume, not VAT area, in colonoscope insertion for the first time.

5. Table 2 –The column percentages are little informative (eg, 91.1% <65years, 8.9% >65 years). Please replace them with row percentages, in order to help the reader to compare at a glance CIT according to different characteristics of patients.

→ **We replaced column percentages with row percentages.**

Minor

1. Abstract: maybe the Authors confused HR with OR? Please correct.

→ **We corrected 'HR' to 'OR'.**

2. Methods – Anthropometrics Measurements. Last line: drop a bracket before "0.95 for men"; replace WC with WHR

→ **We dropped a bracket and corrected 'WC' to 'WHR'. In addition, we are afraid that WHR were classified according to WHO criteria, not previous study. We corrected the sentence.**

Revised in page 6, line 20

Two levels of WHR were classified as follows according to WHO criteria: normal WHR (≤ 0.9 for men, ≤ 0.8

for women) and high WHR (> 0.9 for men, > 0.8 for women).

3. Results – Baseline characteristics. The first part of the sentence is superfluous. The Authors can directly report the result ("23.8% of participants…).

→ **Following your suggestion, we revised the sentence.**

Revised in page 8, line 11

Four hundred (23.8%) of participants required longer than 10 minutes.

4. Text and tables: two decimal places are enough and more readable than three for OR and 95%CI.

→ **We corrected three decimal places to two decimal places for OR and 95% CI.**

5. Table 1. Please add the number and % of cases aged < and > than 65 years.

→ **We added the number and % of cases aged < and ≥ than 65 years in Table 1.**

6. Table 2. I suggest to modify the title as follows: Cecal insertion time according to study variables, with Odd Ratios estimated by multivariate logistic regression analysis

→ **We modified the title following your suggestion.**

7. Table 3. I suggest to modify the title as follows: Cecal insertion time according to study variables, by gender, with p-values estimated by univariate analysis

→ **We modified the title following your suggestion.**

8. Suppl Table 1. I suggest to modify the title as follows: Cecal insertion time according to study variables, by experience of the endoscopist, with Odd Ratios estimated by multivariate logistic regression analysis

→ **We modified the title following your suggestion.**

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Response to Reviewer's Comments

Reviewer's code: 02917331

Dear authors, In this paper entitled "Predictors for difficult cecal insertion in colonoscopy: the impact of obesity indices" the authors attempted to evaluate factors which affect cecal insertion time. This study seems to contain novel aspects, however, statistical concerns are pointed out.

1. Major comment, In Table 3 and Table 4, all statistical analyses are multiple testing. The bonferroni adjustments are applied for analyses.

→ **Thanks for your kind comment. Our analysis was performed by Pearson Chi-squared test for categorical variables in Table 2, 3. We consulted the statistician about our analysis for reinforcing your comment about multiple tests in table 3 and 4. We showed the predictive factors of prolonged cecal insertion time (CIT) in uni- and multi-variate analysis. We were curious about the gender effect on CIT, and so performed the subgroup analysis based on the gender. The statistician responded that our analysis was reasonable process in table 3. And, Bonferroni method was undergo for multiple comparisons for analysis of the dependent continuous variables in more than 3 independent categorical groups after ANOVA test was significant. Bonferroni test could not apply to multivariate analysis like table 4.**

→ **We added new information to table 2, and 3 (post hoc analysis for Pearson Chi-squared test). That presented which groups affected on prolonged cecal intubation time among three independent groups; BMI and VAT with regard to your comment.**

Revised Table (in page 16~17)

Table 2. Cecal insertion time according to study variables, with Odd Ratios estimated by multivariate logistic regression analysis

	Cecal insertion time (min), n (%)		p-value	Multivariate logistic regression analysis OR (95% CI)	p-value
	≤10 (n=1278)	>10 (n=400)			
Age (years)			0.125		
< 65	1164 (76.7)	354 (23.3)			
≥65	114 (71.3)	46 (28.7)			
Gender			0.001		
Male	800 (79.1)	212 (20.9)		Ref	0.047
Female	478 (71.8)	188 (28.2)		1.29 (1.00-1.67)	

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Obesity indices					
BMI (kg/m^2)			<0.001		
< 23	457 (72.2)	176 (27.8)*		1.62 (1.16-2.25)	0.004
23~24.9	388 (83.6)	76 (16.4) **		Ref	
≥25	433 (74.5)	148 (25.5)		1.80 (1.31-2.49)	< 0.001
WHR[a]			0.060		
Normal (<0.95 for men, <0.80 for women)	257 (72.4)	98 (27.6)			
High	1018 (77.2)	301 (22.8)			
WC (cm) [b]			0.316		
Normal (<0.95 for men, <0.80 for women)	1098 (76.6)	335 (23.4)			
High	179 (73.7)	64 (26.3)			
VAT volume (cm^3)			<0.001		
< 500	237 (68.3)	110 (31.7)***		1.50 (1.09-2.07)	0.013
500~1499	906 (78.9)	242 (21.1)		Ref	
≥1500	135 (73.8)	48 (26.2)		1.27 (0.86-1.88)	0.223
SAT volume (cm^3)			0.848		
< 1000	107 (78.1)	30 (21.9)			
1000~1999	831 (75.9)	264 (24.1)			
≥2000	340 (76.2)	106 (23.8)			
History of abdominal surgery			0.626		
No	1077 (76.4)	333 (23.6)			
Yes	201 (75.0)	67 (25.0)			
Constipation			0.112		
No	1148 (76.7)	348 (23.3)			

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Yes	130 (71.4)	52 (28.6)			
Experience			< 0.001		
Attending physicians	833 (80.2)	206 (19.8)		Ref	
Fellow	445 (69.6)	194 (30.4)		1.73 (1.38-2.19)	<0.001
Bowel preparation			0.919		
Excellent to fair	920 (76.1)	289 (23.9)			
Poor to inadequate	358 (76.3)	111 (23.7)			
Diverticulosis			0.099		
No	1199 (75.7)	384 (24.3)			
Yes	79 (83.2)	16 (16.8)			

[a] n=1674

[b] n=1676

[*] p <0.001 compared with BMI 23~24.9 kg/m^2

[**] p <0.001 compared with BMI ≥ 25 kg/m^2

[***] p <0.001 compared with VAT 500~1499 cm^3

BMI = body mass index; WHR = waist-to-hip circumference ratio; WC = waist circumference; VAT = visceral adipose tissue; SAT = subcutaneous adipose tissue; OR = odds ratio; CI = confidence interval

Revised Table (in page 18~19)

Table 3. Cecal insertion time according to study variables, by gender, with p-values estimated by univariate analysis

	Male (n=1012)			Female (n=666)		
	Cecal insertion time (min), n (%)		p-value	Cecal insertion time (min), n (%)		p-value
	≤10 (n=800)	>10 (n=212)		≤10 (n=478)	>10 (n=188)	
Age (years)			0.089			0.619
< 65	726 (90.8)	184 (86.8)		438 (91.6)	170 (90.4)	
≥65	74 (9.3)	28 (13.2)		40 (8.4)	18 (9.6)	
Obesity indices						
BMI (kg/m^2)			0.007			0.013
< 23	202 (25.3)	58 (27.4)		255 (53.3)	118 (62.8) [**]	

23~24.9	261 (32.6)	46 (21.7)*		127 (26.6)	30 (16.0)	
≥25	337 (42.1)	108 (50.9)		96 (20.1)	40 (21.3)	
WHR			0.414			0.332
Normal	118 (14.8)	36 (17.1)		139 (29.1)	62 (33.0)	
High	680 (85.2)	175 (82.9)		338 (70.9)	126 (67.0)	
WC (cm)			0.396			0.508
Normal	768 (96.1)	201 (94.8)		330 (69.0)	134 (71.7)	
High	31 (3.9)	11 (5.2)		148 (31.0)	53 (28.3)	
VAT volume (cm^3)			0.123			0.020
< 500	73 (9.1)	24 (11.3)		164 (34.3)	86 (45.7)***	
500~1499	606 (75.8)	146 (68.9)		300 (62.8)	96 (51.1)	
≥1500	121 (15.1)	42 (19.8)		14 (2.9)	6 (3.2)	
SAT volume (cm^3)			0.511			0.082
< 1000	90 (11.3)	23 (10.8)		17 (3.6)	7 (3.7)	
1000~1999	575 (71.9)	146 (68.9)		256 (53.6)	118 (62.8)	
≥2000	135 (16.9)	43 (20.3)		205 (42.9)	63 (33.5)	
History of abdominal surgery			0.087			0.213
No	687 (85.9)	172 (81.1)		390 (81.6)	161 (85.6)	
Yes	113 (14.1)	40 (18.9)		88 (18.4)	27 (14.4)	
Constipation			0.480			0.350
No	740 (92.5)	193 (91.0)		408 (85.4)	155 (82.4)	
Yes	60 (7.5)	19 (9.0)		70 (14.6)	33 (17.6)	
Experience			<0.001			0.015
Attending physicians	552 (69.0)	115 (54.2)		281 (58.8)	91 (48.4)	
Fellow	248 (31.0)	97 (45.8)		197 (41.2)	97 (51.6)	
Bowel preparation			0.561			0.462
Excellent to fair	561 (70.1)	153 (72.2)		359 (75.1)	136 (72.3)	
Poor to inadequate	239 (29.9)	59 (27.8)		119 (24.9)	52 (27.7)	
Diverticulosis			0.135			0.966
No	734 (91.8)	201 (94.8)		465 (97.3)	183 (97.3)	
Yes	66 (8.3)	11 (5.2)		13 (2.7)	5 (2.7)	

WHR, male n=1009

WC, male n=1011

WHR, female n=665

WC, female n=665

* p = 0.004 compared with ≥ 25 kg/m^2

** p = 0.009 compared with BMI 23~24.9 kg/m^2

*** p = 0.015 compared with VAT 500~1499 cm^3

BMI = body mass index; WHR = waist-to-hip circumference ratio; WC = waist circumference; VAT = visceral adipose tissue; SAT = subcutaneous adipose tissue; OR = odds ratio; CI = confidence interval

2. Minor comment, In Abstract, "hazard ratio [HR]" is miss-typed? "odds ratio [OR]" is correct?
→ We corrected 'HR' to 'OR'.

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Response to Reviewer's Comments

Reviewer's code: 03478442

This is an interesting study about factors influencing the cecal intubation time. It adds to the literature on the subject, despite the fact that some findings were also previously reported by other studies.

1. The window of normal BMI (between 23 and 25 kg/m^2) is very narrow. For obese patients, I think that they should be further classified to overweight and obese to have more information regarding the role of obesity to cecal intubation time. It could be found, for example, that slightly overweight patients (BMI 26-27) have a similar intubation time to regular weight subjects. This is important because the proportion of patients being overweight is very high according to obesity studies.

→ This is the same question as Reviewer 1.

We added these results in the DISCUSSION section of the main manuscript.

Added in page 10, line 20

In our study, when higher BMI (≥ 25 kg/m^2) group was divided into overweight (25~29.9 kg/m^2) and obese (≥ 25 kg/m^2) group, not obese group but overweight group was associated with prolonged CIT in multivariate analysis. Even though high BMI (≥ 30 kg/m2) was not significant association in univariate and multivariate analysis, there was a trend of association with prolonged CIT. The cause of these result might be the low number of high BMI (n=45) (data not shown).

2. It is interesting that older age was a factor of difficulty for fellows but not for experienced endoscopists. Please comment on that.

→ Though we do not know the exact reason for the difference between two groups, it might be caused by lack of skill of fellow. The sentences were modified as follows.

Revised in page 12, line 2

Several studies have reported different results whether older age associate with prolonged CIT. A prospective study by Zuber-jerger et al. showed CIT was not related with age[27]. However, consistent with our results of fellow group, a study for colonoscopy learning curves of gastroenterology fellows reported an older age was associated with a longer insertion time[28]. Length of the entire colon has been reported to increase with age, resulting in increased redundancies and loop formation[29]. Also, decreased elasticity of the colon associated with advanced age predisposes to loop formation during colonoscopy[9]. These might impede the advancement of the colonoscope, especially among fellows who lack the skills.

3. How about discomfort during the procedure? Is there any information on that regarding BMI?

→ **This study includes both sedation and sedation-free participants. Unfortunately, there is no record of patient discomfort. The relationship between sedation dosage and BMI was confirmed indirectly.**

Pearson correlation coefficient between CIT (continuous variable) and sedation dosage (Midazolam dosage, continuous variable) was 0.105 ($p<0.001$). Pearson correlation coefficient between BMI (continuous variable) and sedation dosage (Midazolam dosage, continuous variable) was -0.004 ($p=0.876$). In our study, there was no correlation between BMI and sedation dosage.

It is described as a limitation in the discussion section (in page 12, line 23; Second, factors such as pain tolerance and use of narcotic agents, which may affect difficult colonoscopy, were not assessed).

4. How could you explain that the waist circumference plays no role in cecal intubation time in both men and women?

→ **Following your suggestion, we added the sentences in DISCUSSION section of main manuscript.**

Added in page 11, line 11

A study demonstrated that smaller WC was associated with prolonged CIT. In contrast, consistent with our result, Chung et al. reported that there was no direct correlation between WC and CIT. It might be because WC does not seem to reflect real volume of the peritoneal cavity.

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5. Page 9, last paragraph, please correct: with lower BMI was being associated with a difficult procedure

→ **We corrected the sentence as your mention.**

6. Is there any information about the small number of cases who had a long procedure? Were there any additional factors for a prolonged procedure? That is important because it is different to have a 7 min, a 14 min and a 40 min insertion time for example. Please comment on that if possible.

→ **Due to the limitations of the retrospective study, the reason for prolonged CIT was not documented.**

When the participants were classified into four groups according to CIT (CIT ≤ 7min (n=298, 44.7%), 8-14min (n=275, 41.3%), 15-40min (n=93, 14%), >40min (n=0, 0%)), ninety three patients of CIT more than 15min were all women.

We added these results in the DISCUSSION section of the main manuscript.

Added in page 10, line 1

In addition, ninety three patients of CIT more than 15 min were all women in our study.

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Additional revision

1. We have changed ‘sex’ to ‘gender’ to unify the format.