Cover letter

Dear Editors and Reviewers:

Thank you very much for arranging a timely review for our manuscript (Manuscript NO.: 58303). We have carefully evaluated your and the reviewers' comments and thoughtful suggestions. All of the comments have been carefully addressed and a point-to-point revision was made accordingly. I have highlighted the corrections in the revised manuscript for your review. In the revised version, our manuscript has been carefully edited for typographical and grammatical errors. Please find below the details of our revisions. Like other studies of constipation, we hope our revised manuscript also will be beneficial for further study of in the treatment of internal rectal prolapse in females.

Again, we want to thank you for your effort and help with our manuscript. Should you have any questions, please feel free to contact me at yy_150@126.com.

Very Respectfully,

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Point-by-point rely to reviewers' comments

Reviewer's Number ID: 00503176

Specific Comments to Authors:

My knowledge on the topic addressed is only general - hence my comments are related only to some of the methodological aspects. In this respect I have to briefly summarize the (methodological) essence so that the comments are then perceived in an adequate way. This is an observational study. During a certain period of time, one method was used. Then, a method was improved and subsequently, all patients underwent the new method (surgical procedure). So, it is a non-randomized comparison. It evaluated outcomes after 6 months, 2 years and 5 years post-surgery. Even in a randomized trial, after elapse of such a long time - many things happen with patients that may influence the outcome (ie., post-baseline covariates or confounders) - these are difficult to account for, even in a RCT, yet aline in an observational study.

Often, authors burden studies with many statistical tests - typically - too many. But statistical tests and p.values cannot "fix" some things related to design. In this paper, there are by far too many statistical tests that actually do not mean much. Also, Figures 1-4 and then tables 2 and 3 show more or less the same thing.

Re: We would like to express our sincere thanks to you for carefully and patiently reviewing our manuscript. Thanks for your comments, especially related to the methodological aspects.

My specific (minor) comments are:

1. The authors should report for both group A and group B -how many patients were initially considered for inclusion (to result in the enrolled number of subjects).

Re: Thanks for pointing out it. In the paragraph of "***General information***", we have revised it as "In our study, 140 female patients were initially included, 70 of them were included in group A and another 70 of them were included in group B. Among the 140 patients included in this study, a total of 10, including seven in group A and three in group B, were lost to follow-up. Eventually, the number of analyzable cases was 130, including 63 cases in group A and 67 cases in group B."

2. One table (like the current Table 1) - should show the baseline data. This is ok.

Re: Thanks for your useful suggestions. In Table 1. We have compared the preoperative parameters regarding DIRP, WCS, WIS, GIQLI and BM between the two groups and they are not significantly different between the two groups. We have deleted the baseline data in Table 3, which are the same as the data in Table 1.

3. One Figure, e.g., Figure 1 (A-D) should show the 4 scores over time like mean(SD) or similar - just the RAW data (pre-op, and then at post-op times. Under each time point, the number of considered subjects should be given).

Re: This is our mistake. In the revised manuscript, we have deleted the figures 1-4, which show the same meaning as tables 2 and 3. The paragraph of **"Functional recovery compared between groups:"** has been revised as "The WCS score, WIS score, GIQLI score, and DIRP of group B were significantly better than those of group A 6 months, 2 years after surgery (all $P < 0.001$, Bonferroni) except DIRP at 2 years after surgery, and the improvement became more obvious over time. See Table 3."

4. ANOVA is more or less an appropriate approach. A better one would be a general linear mixed model (it will not "delete" subjects who did not complete all time-points - but will use all data available at each point). The outcome should be "change vs. pre-op score" - adjusted for covariates of at least AGE and BASELINE score.
5. I would restrict the analysis at 2 years. The drop-out and post-baseline events that might have influenced the outcome at 5 years are progressively many - and are not taken into account. So, I would simply have, for each score (difference vs. baseline), a following model: fixed factors: treatment, baseline score, age, time (6 months and 2 years) and time*treatment interection. the result would be a) overall difference between surgeries and b) differences at 6 mo and 2 years (adjusted for multiple comparisons). No other comparisons and tests. Data for 5 year could be reported as descriptive only - statistical tests do not make much sense...when the design is such that the outcomes are most likely confounded by many unmeasured covariates.

Re: Thanks for your constructive suggestions. Following your suggestions, the potential differences between different surgical therapy and the changes of efficacy with time were analyzed by using the generalized linear mixed effect model, with age, time and baseline data as covariables. The baseline data of the two groups were compared by the t-test and $\chi 2$ test. The recovery conditions of the two groups were compared by post-hoc comparisons (Bonfferoni analysis was used for multiple comparisons correction).

We have deleted all the outcome at 5 years after surgery and removed the 5 years to 2 years comparison, the 5 years to 6 months comparison, and the 5 years to preoperative comparison (The details are in the revision of the revised manuscript). Table 1, table 2 and table 3 are modified as follows:

Table 1 Comparison of the basic information between patients with internal rectal prolapse in groups A and B

			Group A (n=63)	Group B (n=67)	P
Patient information	Age	Yr	50.46±13.95	49.90±14.25	0.820
	BMI	kg/m^2	24.70±3.71	24.46±3.24	0.700
Preoperative data	DIRP	cm	3.41±0.27	3.50±0.33	0.093
	WCS	0-30	8.41±3.06	8.30±3.20	0.853
	WIS	0-20	8.75±2.43	8.76±2.28	0.962
	GIQLI	0-144	100.90±5.83	101.16±6.13	0.796
	BM	Number of times/d	3.35±1.15	3.49±1.05	0.459
Intraoperative and postoperative data	Operation time	min	40.35±5.96	50.45±6.52	<0.001
	Intraoperative blood loss	ml	4.63±1.35	8.22±3.67	<0.001
	Time to first passage of feces/flatus	d	2.22±1.01	2.48±0.98	0.144
	Length of hospital stay	d	4.87±1.20	5.58±1.76	0.009
	Complications (Dindo >I)	n (%)	7 (11.11%)	8 (11.94%)	0.882

Table 2 Preoperative and postoperative functional recovery results (mean ± SD)

		Before surgery	6 months after surgery	2 years after surgery	P（Bonferroni）		
					Before surgery vs 6 months after surgery	Before surgery vs 2 years after surgery	6 months after surgery vs 2 years after surgery
Group A (63)	DIRP	3.41±0.27	0.54±0.56	0.75±0.63	<0.001	<0.001	<0.001
	WCS	8.41±3.06	1.33±1.00	2.41±1.16	<0.001	<0.001	<0.001
	WIS	8.75±2.43	5.63±1.80	5.33±1.32	<0.001	<0.001	0.011
	GIQLI	100.90±5.83	104.05±5.88	103.06±5.99	<0.001	<0.001	0.003
Group B (67)	DIRP	3.50±0.33	0.18±0.44	0.61±0.72	<0.001	<0.001	<0.001
	WCS	8.30±3.20	0.51±0.89	1.33±1.11	<0.001	<0.001	<0.001
	WIS	8.76±2.28	3.58±1.22	2.37±0.89	<0.001	<0.001	<0.001
	GIQLI	101.16±6.13	109.67±5.61	117.72±15.29	<0.001	<0.001	<0.001

Table 3 Postoperative functional recovery comparison between the two groups (mean ± SD)

		Group A (n=63)	Group B (n=67)	P (time*treatment)	P (Bonferroni)
DIRP	6 months after surgery	0.54±0.56	0.18±0.44	0.144	<0.001
	2 years after surgery	0.75±0.63	0.61±0.72		0.235
WCS	6 months after surgery	1.33±1.00	0.51±0.89	0.284	<0.001
	2 years after surgery	2.41±1.16	1.33±1.11		<0.001
WIS	6 months after surgery	5.63±1.80	3.58±1.22	0.004	<0.001
	2 years after surgery	5.33±1.32	2.37±0.89		<0.001
GIQLI	6 months after surgery	104.05±5.88	109.67±5.61	<0.001	<0.001
	2 years after surgery	103.06±5.99	117.72±15.29		<0.001
Postoperative recurrence	6 months after surgery	6 (9.5%)	0		0.011
	2 years after surgery	13 (20.63%)	8 (11.94%)		0.178

6. The Discussion should address this point - a) non-randomized setting, b) not accounting for potential post-baseline covariates. The interpretation of the results, should, consequently be - that data are "strongly suggestive" for a superiority of the improved technique - and that a randomized trial with blinded patients and assessors is warranted to confirm this suggestion.

Re: Thanks for your constructive suggestion. In the revised manuscript, we have added following sentences in the discussion according to your

suggestion: “This work is a retrospective non-randomized single-center study and has certain limitations, such as not accounting for potential post-baseline covariates. We will further develop a multicenter randomized controlled study. Meanwhile, we will expand the sample size and go a randomized trial with blinded patients and assessors to further evaluate the efficacy of Integral theory–guided laparoscopic IPFLR combined with PPH.”

Reviewer's Number ID: 02861252

Specific Comments to Authors:
Good work indeed...

Re: We would like to express our sincere thanks to you for carefully and patiently reviewing our manuscript. Thanks for your comments.

Reviewer's Number ID: 05112530

Specific Comments to Authors:
Despite the large number of patients in the main and control groups, the study is retrospective and not randomized, which reduces the level of evidence of the study results. It is recommended in the future to conduct a randomized, and possibly a multicenter study to obtain more reliable results. The authors' conclusions are logical and consistently proved by them in the reviewed article. Given the high level of research, the article is recommended for publication.

Re: Thanks for your constructive suggestions. This work is a retrospective single-center study and has certain limitations. We will further develop a multicenter randomized controlled study to further evaluate the efficacy of Integral theory-guided laparoscopic IPFLR combined with PPH.