Older patients with IBD might have higher risk of Parkinson's disease

We read with interest the study by Villumsen *et al*¹ which reported that patients with IBD had a 22% increased risk of Parkinson's disease (PD) compared with non-IBD individuals. The study supported the theory that intestinal environment could influence the function of central nervous system which was also called the gut-brain axis. Recently, a

meta-analysis by Zhu *et al*² suggested that the overall risk of PD in patients with IBD was significantly higher than controls (OR 1.41; 95% CI 1.19 to 1.66). However, only four studies were included in the meta-analysis. We also noticed a case-control study by Camacho-Soto *et al*³ reporting that the risk of PD was inversely associated with IBD (OR 0.85; 95% CI 0.80 to 0.91), which was not included in the meta-analysis by Zhu *et al*.²

To better understand this issue, we searched the PubMed and Web of Science for cohort and case-control studies investigating associations between IBD and risk of PD published before October 2018. Finally, five studies¹⁻⁵ with totally 9 174 766 participants were included, and we performed a meta-analysis with the software STATA V12.0. The overall results showed that compared with reference individuals, patients with IBD did not have a significantly increased risk of PD (OR 1.19; 95% CI 0.93 to 1.44; $p_{\text{heterogeneity}} < 0.001$), while the results with four cohort studies suggested that patients with IBD had significantly higher risk of PD (OR 1.26; 95% CI 1.17 to 1.35; $p_{\text{heterogeneity}} = 0.84$) (figure 1). Subgroup analysis for different classifications of IBD with all studies suggested that patients with UC or Crohn's disease (CD) did not have higher risk of PD, while the results with cohort studies showed that patients with UC or CD were associated

Figure 1 Forest plot of studies investigating associations between IBD and risk of Parkinson's disease.

Table 1 Subgroup analysis for different IBD and age

Subgroup	Studies (n)	OR	95% CI	P _{heterogeneity}
UC				
Cohort study	3	1.29	1.13 to 1.45	0.58
Case-control study	1	0.88	0.82 to 0.96	—
All studies	4	1.12	0.81 to 1.42	<0.001
Crohn's disease				
Cohort study	3	1.28	1.10 to 1.47	0.60
Case-control study	1	0.83	0.74 to 0.93	—
All studies	4	1.13	0.81 to 1.45	<0.001
Age				
<50 years old	2	1.18	0.73 to 1.62	0.70
≥60 years old	3	1.32	1.16 to 1.47	0.91

with higher risk of PD (table 1). For the age at IBD diagnosis, we also found that patients with IBD in subgroup of '<50 years old' were not associated with higher risk of PD. However, patients with IBD in subgroup of '≥60 years old' had significantly increased risk of PD (OR 1.32; 95%CI 1.16 to 1.47) (table 1).

Our meta-analysis showed that patients with IBD did not have an increased risk of PD; however, subgroup analysis with cohort studies showed that they might be associated with increased risk of PD. PD is a multi-system disorder that occurs as a consequence of degeneration of dopaminergic and non-dopaminergic neurons, and the age has been regarded as an important risk factor for PD.⁷ In this study, we found that older patients with IBD had higher risk of PD which suggested that the age at IBD diagnosis might be a risk factor of PD. We also noticed that some studies presented the medication-associated side effects which resembled parkinsonism in the older population.^{8,9} Therefore, it is necessary to take it into consideration whether older people will take more

medications, and whether these medications lead to a higher risk of PD also needs further studies to verify in the future.

In conclusion, based on the majority of included studies, patients with IBD, especially for those with later age, seemed to be associated with increased risk of PD. However, whether patients with IBD with younger age have higher risk of PD needs further well-designed observational studies to verify in the future.

Qian-Yi Wan, Rui Zhao, Xiao-Ting Wu

Department of Gastrointestinal Surgery, West China Hospital, Sichuan University, Chengdu, China

Correspondence to Professor Xiao-Ting Wu, Department of Gastrointestinal Surgery, West China Hospital, Sichuan University, Chengdu 610041, China; 2687183445@qq.com

Contributors Q-YW and RZ contributed equally in this study. Q-YW and RZ wrote the manuscript under the guidance of X-TW. All authors have read the manuscript and X-TW has approved the final manuscript.

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