Investigating the Causal Links between COVID-19 and Pancreatitis by Bidirectional Mendelian Randomization

Xiaoqing Xu[1], Chang Qu[1], Jiongdi Lu[1], Zhen Fang[1], Wentong Mei[1], Yixuan Ding[1], Jia Li[1], and Fei Li[1]

[1]Capital Medical University

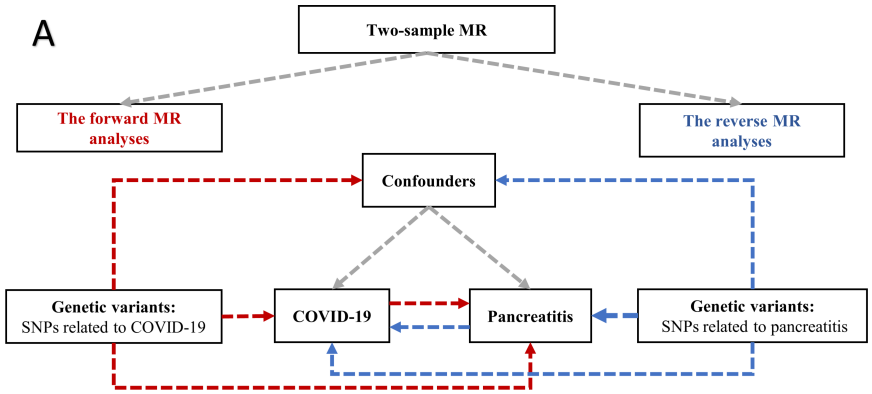
July 19, 2023

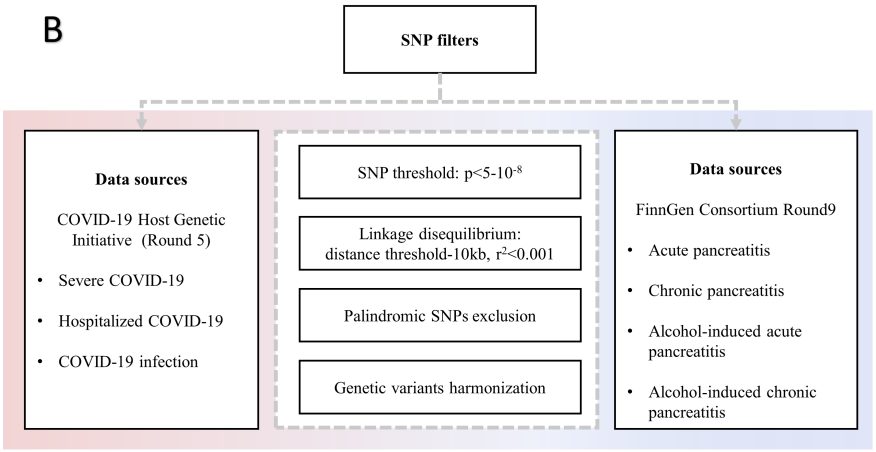
Abstract

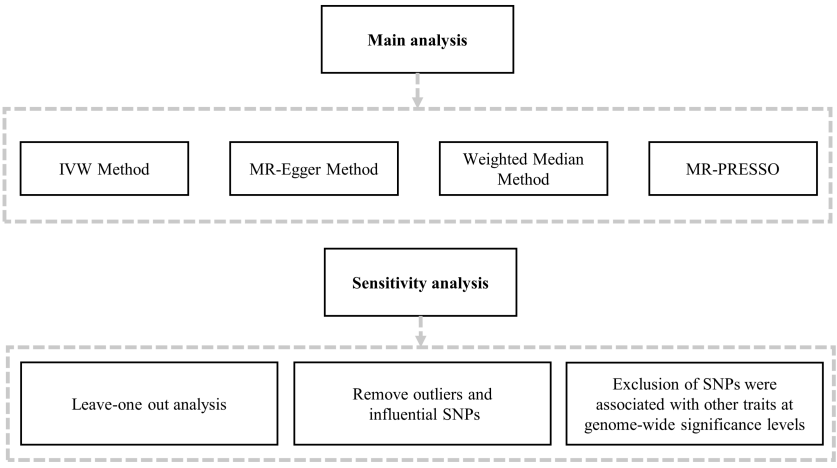
Objective The immune response is a double-edged sword, and COVID-19 shares similarities with pancreatitis in terms of natural immune response, immune storm, and multi-organ involvement. However, whether a causal association between them remained unclear. This study aimed to investigate the potential causal association between COVID-19 and pancreatitis using a bidirectional Mendelian Randomization (MR) approach. **Methods** The study analyzed three variables related to COVID-19 (severity, hospitalization, and susceptibility) with a sample size ranging from approximately 1,059,456 to 1,557,411. Additionally, four types of pancreatitis (acute, chronic, alcohol-induced acute, and chronic) were examined, with a sample size ranging from 337,126 to 377,277. Causal associations were estimated using inverse-variance weighted (IVW), median weighted, and MR-Egger methods. **Results** The IVW model indicated potential causal associations between genetic susceptibility to severe and hospitalized COVID-19 and a decreased risk of acute pancreatitis (OR = 0.914, p = 0.01; OR = 0.884, p = 0.008) and alcohol-induced chronic pancreatitis (OR = 0.852, p = 0.013; OR = 0.768, p = 0.002), including chronic pancreatitis. Inconsistent associations were observed between IVW and sensitivity analyses in acute and chronic pancreatitis of severe and hospitalized COVID-19. Conversely, no significant associations were found between pancreatitis traits and COVID-19-related variables in reverse MR analysis. No heterogeneity or pleiotropy was found. **Conclusions** Host genetic liability to severe and hospitalized COVID-19 was causally associated with declining risk of alcohol-induced chronic pancreatitis, while no significant association was observed for pancreatitis on COVID-19 outcomes. This study has significant implications for unraveling their pathogenesis and guiding clinical management.

Hosted file

`Manuscript.docx` available at https://authorea.com/users/640815/articles/655489-investigating-the-causal-links-between-covid-19-and-pancreatitis-by-bidirectional-mendelian-randomization

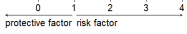






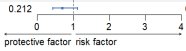
Outcome	Method	nSNP	p	OR(95%ci)	Heterogeneity.test_.p	MR_Egger.intercept.test_.p	MR_PRESSO.global.test_.p
Acute pancreatitis	IVW	5	0.685	1.05(0.82 to 1.34)	0.19	0.572	0.287(raw, 0 outliers)
	Weighted median	5	0.960	0.99(0.72 to 1.37)			
	MR Egger	5	0.665	0.81(0.34 to 1.93)			
Chronic pancreatitis	IVW	5	0.283	1.31(0.80 to 2.17)	0.037	0.662	0.101(raw, 0 outliers)
	Weighted median	5	0.933	1.02(0.62 to 1.68)			
	MR Egger	5	0.487	1.90(0.39 to 9.34)			
Alcohol-induced acute pancreatitis	IVW	5	0.775	0.91(0.49 to 1.70)	0.074	0.636	0.149(raw, 0 outliers)
	Weighted median	5	0.806	0.89(0.37 to 2.15)			
	MR Egger	5	0.616	0.46(0.03 to 6.98)			
Alcohol-induced chronic pancreatitis	IVW	5	0.405	0.83(0.53 to 1.30)	0.107	0.798	0.227(raw, 0 outliers)
	Weighted median	5	0.900	0.96(0.49 to 1.88)			
	MR Egger	5	0.957	1.06(0.17 to 6.72)			

p<0.05 was considered statistically significant



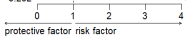
Outcome	Method	nSNP	p	OR(95%cl)	Heterogeneity.test_.p	MR_Egger.intercept.test_.p	MR_PRESSO.global.test_.p
Acute pancreatitis	IVW	6	0.008	0.88(0.81 to 0.97)	0.546	0.287	0.383(raw, 0 outliers)
	Weighted median	6	0.317	0.94(0.83 to 1.06)			
	MR Egger	6	0.837	0.97(0.72 to 1.29)			
Chronic pancreatitis	IVW	6	0.120	0.91(0.80 to 1.03)	0.92	0.301	0.487(raw, 0 outliers)
	Weighted median	6	0.439	0.94(0.80 to 1.10)			
	MR Egger	6	0.709	0.92(0.63 to 1.36)			
Alcohol-induced acute pancreatitis	IVW	6	0.070	0.81(0.64 to 1.02)	0.566	0.92	0.946(raw, 0 outliers)
	Weighted median	6	0.098	0.79(0.60 to 1.04)			
	MR Egger	6	0.287	0.66(0.34 to 1.28)			
Alcohol-induced chronic pancreatitis	IVW	6	0.002	0.77(0.65 to 0.91)	0.693	0.406	0.622(raw, 0 outliers)
	Weighted median	6	0.023	0.78(0.63 to 0.96)			
	MR Egger	6	0.212	0.70(0.43 to 1.12)			

p<0.05 was considered statistically significant



Outcome	Method	nSNP	p	OR(95%cl)	Heterogeneity.test_.p	MR_Egger.intercept.test_.p	MR_PRESSO.global.test_.p
Acute pancreatitis	IVW	8	0.010	0.91(0.85 to 0.98)	0.651	0.745	0.764(raw, 0 outliers)
	Weighted median	8	0.102	0.93(0.85 to 1.01)			
	MR Egger	8	0.295	0.88(0.71 to 1.09)			
Chronic pancreatitis	IVW	8	0.048	0.91(0.83 to 1.00)	0.353	0.45	0.078(raw, 0 outliers)
	Weighted median	8	0.210	0.92(0.81 to 1.05)			
	MR Egger	8	0.384	0.86(0.64 to 1.17)			
Alcohol-induced acute pancreatitis	IVW	8	0.642	0.96(0.80 to 1.14)	0.587	0.7	0.673(raw, 0 outliers)
	Weighted median	8	0.381	0.90(0.72 to 1.13)			
	MR Egger	8	0.904	0.97(0.58 to 1.66)			
Alcohol-induced chronic pancreatitis	IVW	8	0.013	0.85(0.75 to 0.97)	0.385	0.481	0.481(raw, 0 outliers)
	Weighted median	8	0.032	0.82(0.68 to 0.98)			
	MR Egger	8	0.292	0.79(0.53 to 1.18)			

p<0.05 was considered statistically significant



Hosted file

Table 1.docx available at https://authorea.com/users/640815/articles/655489-investigating-the-causal-links-between-covid-19-and-pancreatitis-by-bidirectional-mendelian-randomization

Hosted file

Table 2.docx available at https://authorea.com/users/640815/articles/655489-investigating-the-causal-links-between-covid-19-and-pancreatitis-by-bidirectional-mendelian-randomization