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Correlation between Body Mass Index and Perianal Abscess Hazards: A Mendelian Randomization Investigation

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Abstract

Background: Perianal abscess is an infectious disease that frequently impacts the perianal area. For assessing weight and weight gain, body mass index, or BMI, is a commonly used statistic. Although there is evidence linking obesity to several medical conditions, the relationship between BMI and perianal abscess remains unclear. Whether BMI influences the likelihood of a perianal abscess remains under discussion.

Methods: A two-sample Mendelian Randomization (MR) study was conducted using the weighted average, weighting the median, Weighted Inverse-Variance Weighted (IVW), and MR-Egger regress approaches. Using the accessible to everybody summarized collections of GWAS meta-analyses for BMI among people of South Asian descent (n=8,658) as the being exposed, a Genome-Wide Association Experiment (GWAS) for anal and rectal abscess from people who are involved in the Open GWAS database (total n=183710; case=1 287, control =182423) was applied as the outcome.

Results: We used GWASs to find 29 Single Nucleotide Polymorphisms (SNPs) of genome-wide relevance, using BMI as the variable in question. The IVW technique indicates that there is not enough information to determine a cause-and-effect link among BMI and perianal abscess (Beta= -0.093, SE=0.097, P=0.340). An analysis of MR-Egger regression revealed a lack of causality among BMI and perianal abscess (Beta= -0.254, SE=0.177, P=0.162). The analysis also showed that directed multiplication was improbable to be influencing the results (intercept = 0.024; P=0.285). Furthermore, there is no proof that a link involving BMI and perianal abscess exists according to the weighted mean (Beta= -0.207, SE=0.182, P=0.813) or weighted median (Beta= -0.126, SE=0.139, P=0.363). The funnel plot and the Cochran's Q test, which also revealed no evidence of diversity or imbalances, demonstrated that there had been no direction pleiotropy. In summary, there was insufficient data from the MR the outcomes of analysis to substantiate the theory linking a greater BMI with a higher incidence of perianal abscess.

Keywords: BMI; Perianal abscess; Mendelian randomization

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Introduction

An infectious condition that frequently affects the perianal area is a perianal abscess. Infection or blockage of the perianal glands is the cause [1]. The quality of life for those who have a perianal abscess can be greatly impacted by the extreme pain, swelling, and inflammation that can result from it [2]. Body Mass Index (BMI) is a commonly used metric to evaluate weight and obesity. A person's weight was determined by dividing height squared. A Body Mass Index (BMI) >30 is considered obese. The chance of developing chronic illnesses, including diabetes, cardiovascular disease, and several types of cancer, has been linked to obesity [3,4]. The connection between BMI and perianal abscess is not well understood despite the fact that obesity is linked to a number of health problems. Numerous factors such as infection, trauma, and the state of the local immune system contribute to the development of perianal abscesses. It remains debatable whether BMI affects the risk of perianal abscesses.

Mendelian randomization research methodology will be used in this study to obtain more insights into the causal association between BMI and perianal abscess. By using a random distribution of genotypes to mimic the features of a randomized controlled trial, Mendelian randomization lessens the influence of environmental and genetic influences on the results [5]. When exposure

and outcome data were measured in separate samples, a two-sample MR was used to assess causal effects [6]. The BMI of the participants, frequency of perianal abscesses, and other pertinent variables were ascertained through data collection from a large-scale population cohort. Long-term follow-up observations will be carried out after the participants are arbitrarily assigned to the high or normal BMI groups. To assess the effect of elevated BMI on the risk of perianal abscess, a thorough review of clinical data, lifestyle choices, genetic information, and other relevant variables will be conducted, followed by a statistical analysis.

The findings of this study should add to the body of knowledge on the connection between perianal abscesses and BMI. These results provide more detailed advice for managing obesity and direct preventive and treatment strategies for perianal abscesses. Additionally, in an effort to lower the frequency and related dangers of perianal abscess, the findings of this study may have significant effects on individual healthcare management and public health policies.

Procedure

Data sources and genetic variant selection

The MRC Integrative Epidemiology Unit (IEU) at the University of Bristol produced the Open Genome-Wide Association Studies (OpenGWAS) database. The extensive collection of manually selected GWAS summary datasets is known as OpenGWAS. The datasets are accessible to the general public and can be obtained as open-source files or by running a database query to retrieve the entire dataset (https://gwas.mrcieu.ac.uk/) [7,8].

We used publicly available summary statistics datasets from Genome-Wide Association Studies (GWAS) meta-analyses to obtain information on Body Mass Index (BMI) in 8,658 people of South Asian descent (GWAS ID: ukb-e-23104_CSA). We performed a two-sample Mendelian Randomization (MR) study using genetic variations linked to BMI as Instrumental Variables (IVs) and a p-value threshold of 1.00E-05. After searching for GWAS information on BMI, we obtained summary data (beta coefficients and standard errors) for 29 Single Nucleotide Polymorphisms (SNPs) that were connected to BMI. These were named IVs. In addition, we acquired publicly accessible summary statistical information from a GWAS on anal and rectal abscesses from participants in OpenGWAS (total n=183 710; cases=1 287, controls =182 423; GWAS ID: finn-b-K11_ABSCANAL) (Table 1).

Comparative mendelian randomization statistical analysis

Genetic variations must be associated with exposure, but they could not be confounding factors, according to Mendelian randomization analysis [9]. We ensured that this was followed by a three-step procedure. Prior to any other study, we evaluated the correlation between every Single Nucleotide Polymorphism (SNP) and BMI. In the second step, we examined the relationship between each SNP and perianal abscess risk. In conclusion, we used Mendelian randomization analysis to aggregate these results and determine the objective causal relationship between BMI and the incidence of perianal abscess. We utilized summary statistics from several Genome-Wide Association Studies (GWASs), which involved applying the two-sample Mendelian randomization method [10]. Utilizing this method enables us to calculate the causative influence of exposure (BMI) on the result (perianal abscess). In our research, we employed 29 SNPs as IVs and summarized the BMI and perianal abscess data from GWASs (Table 2).

The Wald ratio estimates of the causal effect derived from various genetic variations were combined using the Inverse-Variance Weighted (IVW) method, which was used in this study and applied a meta-analysis approach [11]. In cases where every genetic variant meets the requirements for an instrumental variable, it offers a consistent estimate of the causal effect of the exposure variable on the output. Two more techniques, MR-Egger regression and weighted median estimator, were employed to address potential pleiotropy, in which genetic variants may affect many variables. Using summary data estimations of the causal effects of individual variations, MR-Egger regression introduces a bias parameter to account for imbalanced pleiotropy [12]. This was done by performing a weighted linear regression of the gene-outcome coefficients on the gene-exposure coefficients, where the estimate of the causal influence was represented by the slope. The mean horizontal pleiotropic effect across genetic variations was estimated using the intercept [13]. However, even in cases where genetic variants account for up to 50% of the data and are therefore invalid instrumental variables, the weighted median estimator yields a consistent estimate of the causal effect [14]. Compared with the MR-Egger analysis, it maintains higher estimates of precision. Statistical significance was set at $P<0.05$. Mendelian randomization analyses were carried out on the MR Base platform (R Version: 4.0.3), App Version: 1.4.3 8a77eb (October 25, 2020) [8].

Sensitivity testing and heterogeneity

Using Cochran's Q-statistics [15] and the I^2 statistic [16,17], we examined the heterogeneity across Single Nucleotide Polymorphisms (SNPs). Furthermore, a "leave-one-out" analysis was carried out to investigate the possible impact of particular SNPs on causal association [18].

Result

Research that was part of the meta-analysis.

Mendelian randomization supporting variables

From Genome-Wide Association Studies (GWASs) on BMI, we identified a group of 29 independent SNPs as IVs in our analysis. Each SNP was found to have a substantial genome-wide association with BMI (Table 2 and Figure 1). Positive relationships were found for all 29 SNPs when evaluating their relationship with perianal abscess; however, these associations were not statistically significant (Table 2). Approximately 0.23% of the variance in exposure was explained by the genetic variants employed as IVs (as shown by the R2 statistic). The F statistic, which measures the strength of IVs, was significant because it was either greater than or equal to 10 for each unique variety. A "weak IV" is often thought to be indicated by an F value less than 10. Therefore, a weak instrument bias was unlikely to have occurred in our analysis.

Based on our Mendelian randomization study, these results generally show that the SNPs that were chosen to be IVs showed significant relationships with BMI and very little instrument bias. This suggests that the SNPs are appropriate for use as IVs.

Findings from Mendelian randomization

The causal relationship between BMI and perianal abscess was not supported by the IVW method (beta= -0.093, SE=0.097, P=0.340; Table 2 and Figure 1, 2). This indicates that directional pleiotropy was unlikely to bias the results; the intercept in the MR-Egger test, which represents the average pleiotropic effect across the genetic

Table 1: Studies and datasets used in the research.

Variants	Variants content	GWAS ID	nCase	Sample Size	SNP	First Author	Consortium	year	Population Studied
Exposure	Body Mass Index (BMI)	ukb-e-23104_CSA	8658	8658	9811391	Pan-UKB team	NA	2020	South Asian/Males and Females
Outcome	abscess of anal and rectal regions (perianal abscess)	finn-b-K11_ ABSCANAL	1287	183710	16380365	NA	NA	2021	European/Males and Females

BMI: Body Mass Index; GWAS: Genome-Wide Association

Table 2: BMI's causal relationship with perianal abscess risk is estimated using MR estimations from each technique.

MR method	nSNP	Beta	SE	P-val	OR	Low 95%	Up 95%
MR Egger	29	-0.254	0.177	0.162	0.776	0.549	1.097
Weighted median	29	-0.126	0.139	0.363	0.881	0.672	1.157
Inverse variance weighted	29	-0.093	0.097	0.34	0.911	0.754	1.102
Weighted mode	29	-0.207	0.181	0.265	0.813	0.57	1.162

Beta: Beta Coefficient; MR: Mendelian Randomization; SE: Standard Error; SNP: Single Nucleotide Polymorphism

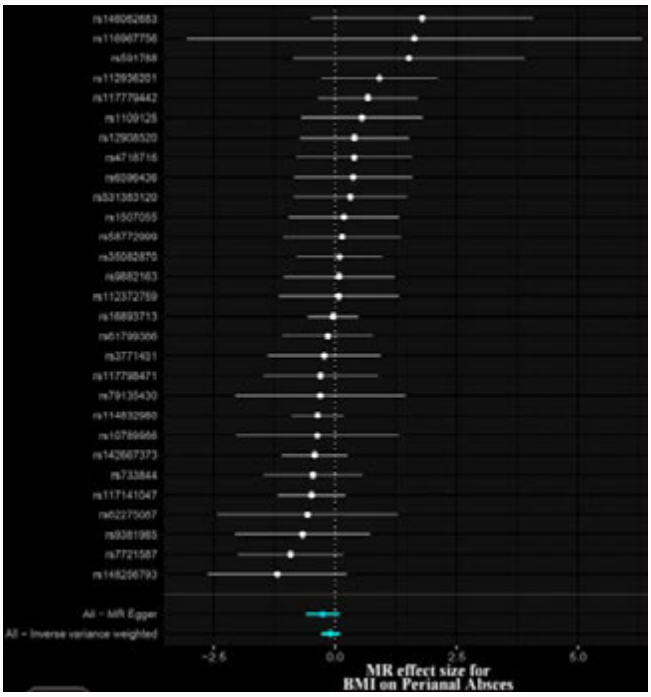

Figure 1: Graph representing a forest of Single Nucleotide Polymorphisms (SNPs) linked to perianal abscess risk and Body Mass Index (BMI). Results from the MR-Egger test and the IVW method are indicated by red lines.

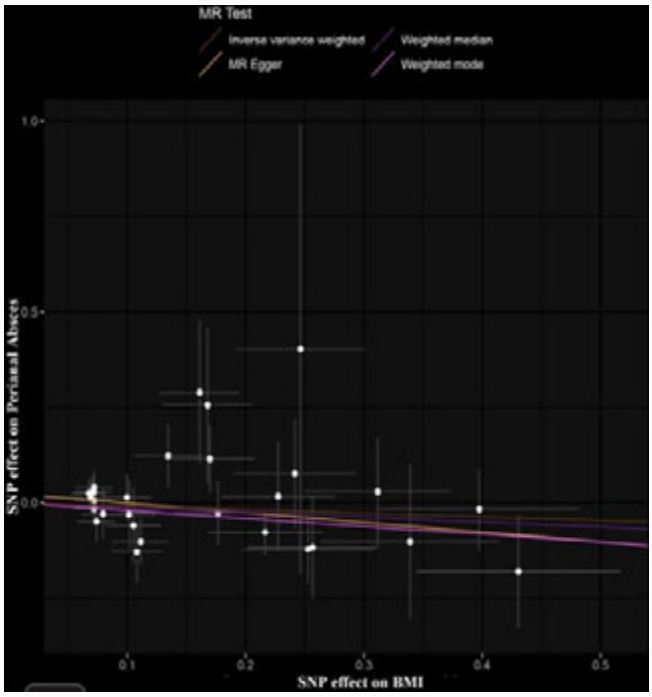

Figure 2: Genomic connections with body mass index *vs.* those with perianal abscess are displayed in scatter plot form. For every technique, the causal relationship is represented by the slope of the line. Weighted estimates are shown by the blue line, inverse-variance weighted estimate, weighted median estimate, Mendelian randomization-Egger estimate, and weighted mode estimate, respectively, colored in dark blue and dark green.

variants (the average direct effect of a variant with the outcome), was not significantly different from zero (intercept= 0.024; P=0.285). Additionally, the MR-Egger analysis, which is displayed in Table 2 and Figure 1, 2, did not demonstrate a causal relationship between BMI and perianal abscesses. Furthermore, neither the weighted mode nor the weighted median techniques (as indicated in Table 2 and Figure 2) produced any proof of a causative relationship between BMI and perianal abscess. The weighted median approach showed beta= -0.207, SE=0.182, P=0.813. The correlations between BMI and perianal abscess were noteworthy because they held true for the weighted mode, weighted median, and MR-Egger approaches. A possible causal relationship between BMI and perianal abscess was not supported by the MR analysis findings.

Sensitivity testing and heterogeneity

When Cochran's Q test was used to evaluate the degree of heterogeneity across instrumental variable estimates derived from individual genetic variations, the findings showed no statistically significant heterogeneity (Table 3 and Figure 3). Low heterogeneity indicates higher reliability of the MR results. Heterogeneity is the variability in causal estimates derived from each SNP. Further corroborating the higher dependability of MR estimates is the minimal heterogeneity shown by I^2 values (Table 3). To assess each SNP's impact on the final IVW point estimate, a "leave-one-out" study was performed. No single genetic variant was responsible for the overall outcome, as the data showed that no single SNP had a substantial impact on the IVW point estimate. There was no discernible asymmetry in the funnel plot (Figure 4), which evaluated publication bias and directional horizontal pleiotropy. The lack of bias resulting from directed horizontal pleiotropy was further demonstrated using the MR-Egger regression test, which similarly revealed no signs of asymmetry. All of the following when combined: The low I^2 values, the "leave-one-out" analysis results, the lack of asymmetry in the

Table 3: Heterogeneity and sensitivity results.

	Methods	Q	df	Q-val	I²
Heterogeneity test	MR Egger	22	27	0.738	0.227
	Inverse variance weighted	23.19	28	0.724	0.207
Sensitivity test	Egger regression intercept	Standard error		Directionality P-value	
	0.024	0.022		0.285	

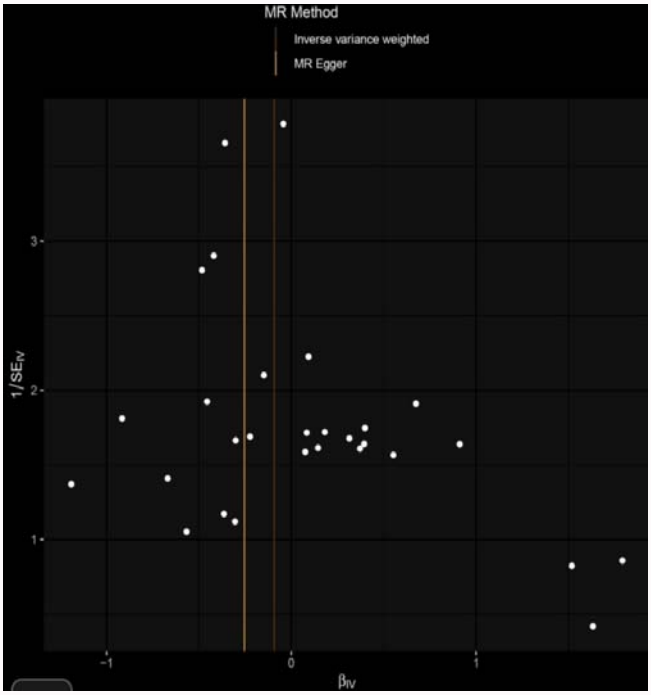

Figure 3: Analyze heterogeneity using a funnel plot. The dark blue line indicates the Mendelian randomization-Egger estimate, and the blue line indicates the inverse-variance weighted estimate.

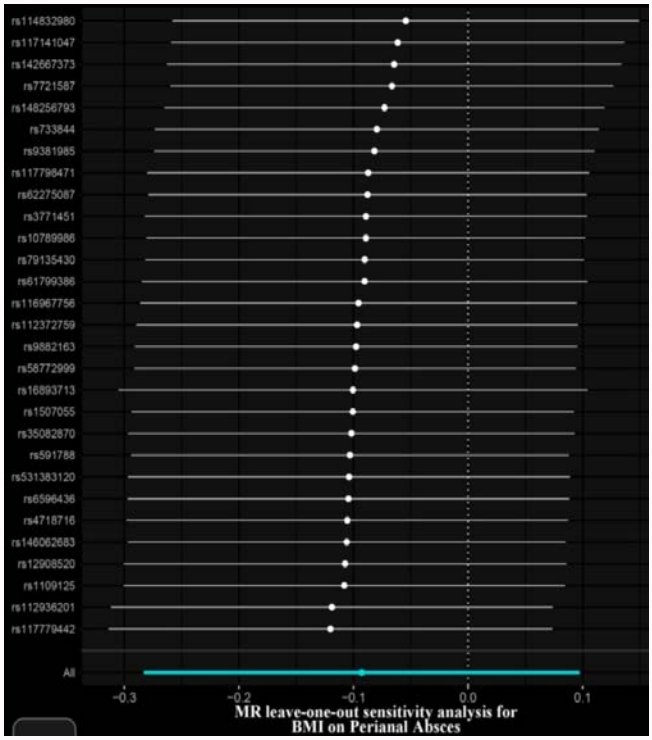

Figure 4: SNPs linked to BMI and the incidence of perianal abscesses are left out. The results of the IVW MR approach, which was used to evaluate the causal influence of BMI on perianal abscess while excluding specific SNPs, are represented by each black point.

MR Egger regression test and funnel plot, the absence of significant heterogeneity, and the assurance about the reliability of the MR estimates all help to allay worries about possible biases in the analysis.

Discussion

Obesity may increase the risk of perianal abscess [2]. However, it is unclear whether obesity and perianal abscesses are related. Using Magnetic Resonance Imaging (MR), we sought to identify any possible links between Body Mass Index (BMI) and perianal abscess. Twenty-nine independent SNPs found by GWASs on BMI were used in this study as IVs. There is insufficient evidence to establish a causal link between BMI and perianal abscess. A reliable MR analysis depends on the selection of strong instrumental factors. All 29 SNPs that were employed as IVs in this investigation showed substantial genome-wide correlations with BMI, indicating that they are suitable for use as instrumental variables. The F-statistics further reinforced the robustness of our IVs by showing a minimal risk of mild instrument bias. To increase the validity of MR analysis, these results emphasize the importance of carefully choosing and validating the instrumental factors.

There was no evidence of a causative relationship between BMI and perianal abscess using the IVW approach, which aggregates estimates from individual SNPs. Likewise, no causal association was found by MR-Egger regression analysis, which considers probable directional pleiotropy. Directional pleiotropy is unlikely to have skewed the results, as indicated by the lack of significant intercepts in the MR-Egger test. Moreover, there was no proof of a causal relationship using weighted median or weighted mode techniques. Our MR estimations are reliable because there was no significant heterogeneity, as shown by the I^2 values and Cochran's Q test. By confirming that no single SNP significantly affected the aggregate IVW point estimate, the "leave-one-out" study further demonstrated that no single variant was responsible for the observed outcomes. The lack of directional horizontal pleiotropy and publication bias are indicated by the non-significant intercept in the MR-Egger test and absence of asymmetry in the funnel plot, respectively.

Our study had several strengths. As instrumental variables, we first used a large range of independent genetic variants to reduce confounding and boost the accuracy of the MR estimations. To evaluate the strength of our conclusions and reduce bias, we performed heterogeneity tests and sensitivity analyses. Furthermore, our results were more reproducible and broadly applicable due to the large sample size and utilization of publicly available summary statistics from GWASs. Finally, to the best of our knowledge, this is the first study of its kind on the causal link between BMI and perianal abscess. However, it is important to recognize that our study also has

limitations. First, hereditary factors affect Body Mass Index (BMI). The combined effects of known genetic loci account for less than 2% of the inter-individual variability in BMI, notwithstanding the effectiveness of Genome-Wide Association Studies (GWAS). Second, variations in obesity and body composition were linked to age and sex. Karin et al. demonstrated that abscesses are more common in men and younger people than in the elderly [2]. Subsequent MR investigations are necessary for various groups, because selection bias and ethnicity may influence causality.

However, there is no proof that perianal abscess and BMI are causally related, according to our Mendelian randomization analysis. These results imply that variables other than BMI may be more important in the development of perianal abscesses. Future studies should investigate other risk factors and mechanisms involved in its pathogenesis to provide a more thorough understanding of the etiology of perianal abscesses. Moreover, rather than concentrating only on lowering BMI, interventions and preventive measures should emphasize holistic management methods that target a variety of risk variables, given the multifactorial nature of perianal abscesses.

Conclusion

MR stands for Mendelian Randomization; IVW stands for Inverse-Variance Weighted; GWAS stands for Genome-Wide Association Studies; SNP stands for Single Nucleotide Polymorphisms; and OpenGWAS is an acronym for Open Genome-Wide Association Studies.

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