

ORIGINAL ARTICLE

Association between IGFBP1 and Lung Cancer Risk: Evidence from a Mendelian Randomization Analysis

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ABSTRACT

Background: Reliable biomarkers for lung cancer risk assessment remain limited. Insulin-like growth factor-binding proteins (IGFBPs) are involved in multiple biological processes and may have clinical relevance in tumor development. This study aimed to evaluate the association between IGFBP family members, with particular attention to insulin-like growth factor-binding protein 1 (IGFBP1), and lung cancer risk using a genetic approach.

Methods: Summary statistics from genome-wide association studies (GWAS) for IGFBPs and lung cancer were obtained from publicly available databases. A two-sample Mendelian randomization (MR) analysis was performed to explore potential associations. The inverse variance weighted (IVW) method was used as the primary analysis, with complementary approaches applied to ensure robustness. Sensitivity analyses were conducted to assess heterogeneity and potential pleiotropy.

Results: Genetically predicted IGFBP1 levels were significantly associated with lung cancer risk. Higher IGFBP1 levels were linked to a modest reduction in lung cancer risk (OR = 0.9989, 95% CI: 0.9981 - 0.9998, p = 0.0126). No significant associations were observed for other IGFBP family members. The results were consistent across analytical methods, and no evidence of heterogeneity or horizontal pleiotropy was detected.

Conclusions: Genetically predicted higher IGFBP1 levels were associated with a reduced risk of lung cancer. These findings provide supportive genetic evidence for the potential involvement of IGFBP1 in lung cancer susceptibility, although further mechanistic and clinical studies are needed for validation.

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Supplementary Data

Table S1. The details of IGFBP1 SNPs in Mendelian randomization analysis.

SNPs	other_allele. ex- posure	effect_allele. outcome	other_allele. outcome	beta.ex- posure	beta.out- come	eaf.exposure	eaf.out- come	remove	pos	samplesize. outcome	outcome
rs10430616	A	G	A	G	-0.1155	0.00011757	0.63447	0.632724	10	0.00020161	0.56
rs112254333	A	G	A	G	0.2291	9.56E-05	0.06693	0.066989	17	0.000388141	0.81
rs115087186	G	C	G	C	-0.5124	0.000707466	0.01318	0.011637	4	0.000940791	0.450001
rs117514824	A	G	A	G	0.2378	-4.86E-05	0.0633	0.058828	7	0.000418795	0.91
rs12231808	A	G	A	G	0.2572	-0.00026413	0.0511	0.048828	12	0.000476024	0.58
rs12768580	G	A	G	A	0.1415	0.000149908	0.29368	0.279922	10	0.000228432	0.51
rs144975238	A	G	A	G	-0.261	0.000467249	0.05461	0.042942	21	0.00049979	0.35
rs1507883	G	A	G	A	-0.1633	0.00018318	0.14481	0.142928	8	0.000278429	0.51
rs3128242	A	G	A	G	0.1388	-0.000459378	0.21845	0.208455	10	0.000247749	0.064
rs555183057	C	T	C	T	0.304	-4.68E-05	0.03754	0.039915	15	0.000498419	0.93
rs6430077	T	C	T	C	-0.461	0.000239213	0.01693	0.014704	2	0.000824303	0.77
rs66964437	T	C	T	C	0.4304	-0.000719091	0.01706	0.017808	8	0.000734093	0.33
rs72700329	C	G	C	G	-0.2991	0.000855361	0.03742	0.035756	4	0.000528569	0.11
rs73975446	G	T	G	T	0.3643	-0.000337623	0.02417	0.026313	17	0.000608491	0.58
rs76258709	T	A	T	A	0.192	-0.000491865	0.11953	0.106402	8	0.000332736	0.14
rs792048	G	A	G	A	0.11	-0.000123803	0.55203	0.549867	2	0.000195798	0.53

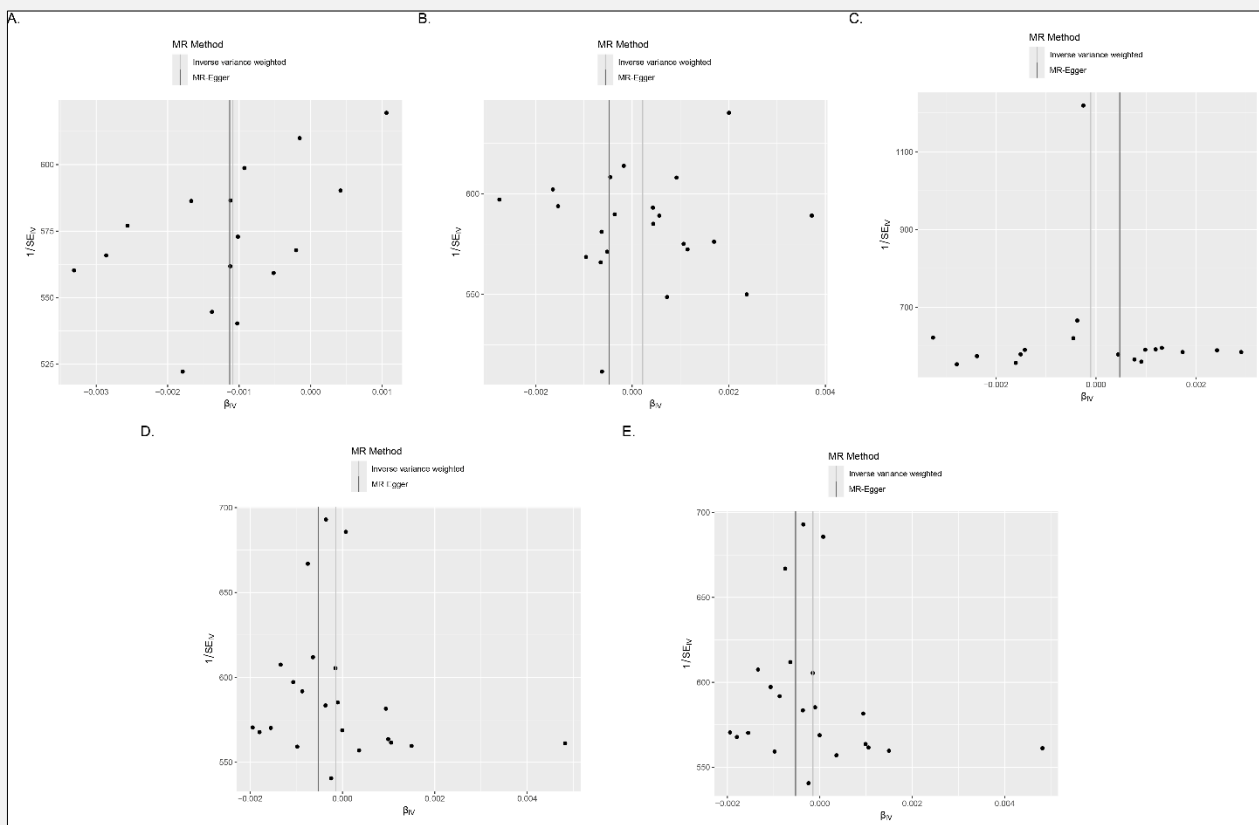


Figure S1. Funnel plots of insulin-like growth factor binding proteins.

A: IGFBP1, B: IGFBP2, C: IGFBP3, D: IGFBP6, E: IGFBP7.

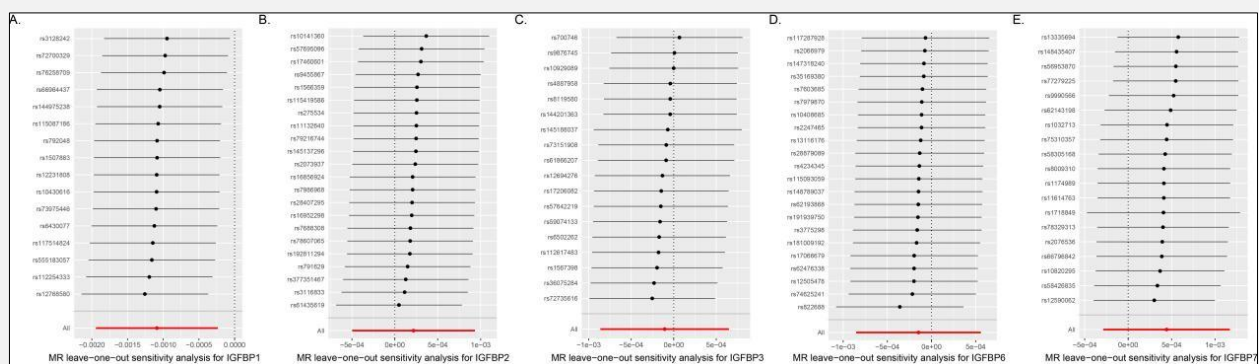


Figure S2. The result of leave one out of insulin-like growth factor binding proteins.

A: IGFBP1, B: IGFBP2, C: IGFBP3, D: IGFBP6, E: IGFBP7.