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Original article

Alternative splicing of *PSMD13* mediated by genetic variants is significantly associated with endometrial cancer risk

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ABSTRACT

Objective: Accumulating evidence has shown that aberrant alternative splicing events are closely associated with the onset and development of cancer. However, whether genetic variants-associated alternative splicing is linked to risk of endometrial cancer remains largely uncertain.
Methods: We identified single nucleotide polymorphisms (SNPs) locates in the splicing number trait locus (sQTL) of endometrial cancer using the CancerSplicing QTL database. In parallel with bioinformatics analysis, we conducted a case-control study comprising 2,000 cases and 2,013 controls to assess the association between identified SNP which possesses mRNA splicing function and endometrial cancer susceptibility. Furthermore, we used the Kaplan-Meier Plotter, The Human Protein Atlas, SPNR, and Spliceman2 databases for sQTL and differential gene expression analyses to identify the genetic variant which most potentially influence the risk of endometrial cancer through alternative splicing to reveal the potential mechanism by which candidate SNPs regulate the risk of endometrial cancer.
Results: The results indicated that SNP rs7128029 A<G was significantly associated with an increased risk of endometrial cancer (odds ratio=1.384; 95% confidence interval=1.038–1.964). Moreover, the carcinogenic effect of SNP rs7128029 A<G was consistently revealed by propensity matching analysis, an additive model, and a dominant model. Importantly, sQTL analysis showed that SNP rs7128029 could affect the transcriptional modification of *PSMD13* via regulating the exon skipping of *PSMD13*. When the rs7128029 allele was mutated from A to G, the expression of exon 2 of *PSMD13* was markedly lower (p<0.001). Furthermore, compared with participants who had higher *PSMD13* expression, those who had lower *PSMD13* expression had shorter survival times.
Conclusion: These findings suggest that SNP rs7128029-mediated alternative splicing events in *PSMD13* are associated with endometrial cancer risk and may be a potential early screening biomarker for endometrial cancer-susceptible populations.

Keywords: Endometrial Cancer; Alternative Splicing; 26S Proteasome Non-ATPase Regulatory Subunit 13; Single Nucleotide Polymorphism

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
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Synopsis
The AS event mediated by SNP rs7128029 in *PSMD13* is associated with endometrial cancer risk and may be an early screening biomarker and potential target for people susceptible to endometrial cancer.

INTRODUCTION

Endometrial cancer is one of the three major malignancies of the female reproductive tract and mainly affects postmenopausal women [1]. In recent years, epidemiological evidence has shown that the average age of onset of endometrial cancer is 60 years worldwide [2]. In China, the incidence of endometrial cancer was 63.4 per 100,000, and the mortality rate was 21.8 per 100,000 in 2015 [3,4]. Currently, the non-genetic risk factors identified for endometrial cancer include age, exogenous estrogen exposure, and endogenous estrogen (sterilization, early menarche, late onset of menopause, obesity) [5]. However, these traditional risk factors do not fully explain the pathogenesis of endometrial cancer. Several lines of evidence have shown that single nucleotide polymorphism (SNP) factors that predispose patients to endometrial cancer, which is supported by the fact that different SNPs of *DACH1* and *XRCC2* are associated with susceptibility to endometrial cancer [6,7]. Moreover, dysfunctional DNA mismatch repair caused by SNPs also dramatically increases the predisposition to cancers [8]. Thus, genetic variants play an important role in the etiology of endometrial cancer [9,10]. Therefore, it is particularly important to screen for carcinogenic genetic variation in susceptible populations.

Alternative splicing is a key post-transcriptional regulatory mechanism, during which precursor mRNA is spliced and generates multiple mature mRNAs or transcripts that contribute to the same gene producing various proteins with different biological functions [11]. It has been shown that 92–94% of human genes undergo selective splicing [12]. Alternative splicing is thought to be a major driver in the evolution of phenotypic complexity in mammals [13,14]. Up to 30% of disease-related genetic variations result in course of disease by controlling alternative splicing events [15]. Importantly, emerging studies have shown that mutations of target gene resulting in alternative splicing events can influence cancer susceptibility [16]. Similarly, various cancer-associated alternative splicing patterns have been found in multiple cancer tissues [17,18]. Alternative splicing is a fundamental process that affects the initiation and development of various cancers by affecting the biological functions of target gene [19]. Therefore, the targeted detection of cancer-associated mutations that control alternative splicing could be a breakthrough in fully understanding the etiology of cancer.

The Cancer Genome Atlas (TCGA) study of endometrioid and plasmacytoma identified many mutations in several crucial genes involved in cancer etiology, such as *P53*, *PTEN*, *PIK3CA*, *CTNNB1*, *KRAS*, and *POLE*. However, the relationship between these mutations in the indicated genes and susceptibility to endometrial cancer has not been elucidated in detail or with only a limited number of samples [20]. In the present study, we found that a certain alternative splicing in *PSMD13* was strongly associated with endometrial cancer risk by searching the CancerSplicing QTL database. After further screening, we determined that there was a strong positive association between rs7128029 of *PSMD13* and risk of endometrial cancer. Furthermore, we combined UniProt data and TCGA databases to determine whether rs7128029-

related alternative event may affect cancer cell apoptosis by altering the structure of certain proteasomes, thereby increasing the risk of endometrial cancer. Finally, at the population level, we demonstrated that genotypes with GG mutations are more susceptible to endometrial cancer than genotypes with AA mutations. Overall, our study integrated TCGA resources and large-scale epidemiological data and identified that alternative splicing of *PSMD13* serves as a key regulatory mechanism linking generic variants to endometrial cancer risk.

MATERIALS AND METHODS

1. Study population

We conducted a case-control study consisting of 2,000 cases and 2,013 healthy controls were recruited from Affinity Hospital of Zunyi Medical University (including Affinity Hospital of Zunyi Medical University, The Second Affinity Hospital of Zunyi Medical University, Zunyi Materal and Health Care Hospital, and Meitan People's Hsopital) from March 2019 to May 2022. The endometrial cancer diagnosis was confirmed histopathologically or cytologically by at least two local pathologists, according to the World Health Organization classification. All the controls were cancer-free individuals selected from physical examination in the same region during the same period when the patients were recruited. At recruitment, peripheral blood samples were collected and stored in the −80° ultra-low temperature freezer, and demographic characteristics including age, smoking, and drinking were collected based on medical records and interviews of these individuals. All study participants signed an informed consent form and the study was approved by the Ethics Committee of Zunyi Medical University (2022(1-302)). Procedures were conducted in accordance with the Declaration of Helsinki and within institutional guidelines.

2. Selection of SNPs

We downloaded the splicing number trait loci (sQTLs) for endometrial cancer from the CancerSplicingQTL database, a cancer splicing database platform, followed by integrated bioinformatics analysis (http://www.cancersplicingqtl-hust.com/) [21]. Quality control was performed using the 1000 Genomes Project database (phase 1, version 3, 1,092 individuals) and Illumina microarrays. The criteria were Hardy-Weinberg equilibrium (HWE) >0.05, minor allele frequency (MAF) >0.05, and call rate >95%. We then screened SNPs with linkage disequilibrium (LD) >0.75 and |R|>0.75. In total, 545 SNPs were selected for genotyping.

3. SNP genotyping

The Qiagen Blood Kit (Qiagen, Hilden, Germany) was used to extract genomic DNA from peripheral blood lymphocytes. All participants were genotyped using the Illumina Human Omni ZhongHua Bead Chips and HumanOmniExpress chips.

4. Bioinformatics analysis and expression analysis

We performed sQTL analysis using the CancerSplicingQTL database and the Genotype Tissue Expression (GTEx) project (http://www.gtexportal.org/) to assess the correlation between the genotype of candidate SNPs and alternative splicing events of *PSMD13*. We used the Kaplan-Meier (K-M) Plotter website (http://kmplot.com/analysis/) and The Human Protein Atlas (https://www.proteinatlas.org/) to assess the association of *PSMD13* expression on the prognosis of patients with endometrial cancer. Furthermore, we used splice function prediction tools such as SPANR and Spliceman2 to predict the biological outcome when alternative splicing of *PSMD13* happens to screening meaningful alternative splicing event.

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5. Statistical analysis

Demographic variables are presented according to the status of endometrial cancer and compared between groups using the χ^2 test and Student's t-test. The association between candidate SNPs and endometrial cancer risk was estimated using binary logistic regression models to produce a dominance odds ratio (OR) with a 95% confidence interval (CI), after adjusting for age, smoking, and alcohol consumption. Furthermore, we conducted a propensity score-matching (PSM) analysis to reduce the effect of potential confounding factors on the association between SNP rs7128029 and endometrial cancer (caliper width ≤0.1 standard deviations [SDs]). We used different genetic models, including dominant, recessive, and additive genetic models, to further determine the relationship between genetic variants and the risk of endometrial cancer. All multiple comparisons were corrected using the false discovery rate (FDR). In addition, the association of SNP rs7128029 with endometrial cancer susceptibility was stratified according to age (≤50, 51–60, 61–70, ≥71 years), smoking (no/yes), and alcohol consumption (no/yes). The K-M plot was used to determine survival time and was examined using the log-rank test. Forest plots, Sankey diagrams, and K-M plots were plotted using the R software (https://www.r-project.org) (version 4.1.0; The R Foundation, Vienna, Austria). SPSS25.0 (IBM Corporation, Armonk, NY, USA) was used for all analyses, and $p<0.05$ was considered to be statistically significant.

RESULT

1. Study population characteristics

A total of 2,000 cases and 2,013 controls were recruited and the demographic information was showed in **Table 1**. The mean age ± SD of the cases and controls were 59.64±10.49 years and 60.65±9.66 years, respectively. The endometrial cancer patients were more likely to be younger than the control subjects ($p<0.05$). There were no significant differences in smoking and drinking status between the case and control groups. Importantly, the distribution of the different SNP genotypes varied between the case and control groups ($p<0.05$). In particular, participants with the GG genotyping were more likely to be in the endometrial cancer group (56.02%) than those with the AA genotype (43.98%) ($p<0.05$). PSM was performed in terms of age, smoking status, and drinking status. A total of 2,000 cases and 2,000 controls were matched, and the baseline characteristics of the enrolled population after PSM are presented in **Table S1**. To reduce non-random errors, we also performed an inverse probability weighting (IPTW) analysis based on PS (**Table S2**).

Table 1. The characteristics of the endometrial cancer cases and healthy controls

Variables	Cases (n=2,000)	Controls (n=2,013)	p
Age (yr)	59.64±10.49	60.65±9.66	<0.001
Smoking			0.499
Yes	87 (4.4)	79 (3.9)	
No	1,913 (95.6)	1,934 (96.1)	
Drinking			0.997
Yes	446 (22.3)	449 (22.3)	
No	1,554 (77.7)	1,564 (77.7)	
SNP genotype			0.006*
AA	1,326 (48.2)	1,425 (51.8)	
AG	581 (52.9)	518 (47.1)	
GG	93 (57.1)	70 (42.9)	

Values are presented as mean±standard deviation or number (%).
SNP, single nucleotide polymorphism.
*p-value for χ^2 test.

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2. SNP selection and association with endometrial cancer risk

Table S3 lists the associations between the top 10 significant SNPs and endometrial cancer risk. After FDR correction, we found that only SNP rs7128029 in *PSMD13* was significantly associated with susceptibility to endometrial cancer. The splicing events for the top 7 significant SNP-related genes associated with endometrial cancer risk are shown in **Table S4**. The results indicated that SNPs that linked with the risk of endometrial cancer could control splicing events of target genes in different ways, including the substitution of 5' splice sites, the substitution of 3' splice sites, exon skipping, and substitution of terminators and promoters.

In this study, we systematically explored the association of SNP rs7128029 with the risk of endometrial cancer for the following analysis. First, we performed a multivariable logistic regression analysis to estimate adjusted ORs and 95% CI for the association between SNP rs7128029 and risk of endometrial cancer. We determined that the OR of endometrial cancer for SNP rs7128029 was 1.428 (95% CI=1.038–1.964), after adjusting for age, smoking, and alcohol consumption. Second, to exclude the confounding effect of potential confounders, we conducted a PSM analysis and IPTW analyses, which indicated similar results (OR=1.6661; 95% CI=194–2.324) and (OR=1.006; 95% CI=0.803–1.260) (**Table 2**). Third, in the additive model, we found that individuals with the G allele had a higher risk of endometrial cancer compared to those with the A allele (OR=1.428; 95% CI=1.038–1.964). Moreover, AA genotyping showed a stronger inverse association with endometrial cancer risk relative to the GG genotype in the dominant model (OR=1.232; 95% CI=1.078–1.408) (**Table 3**).

We further explored the susceptible population regarding the association of SNP rs7128029 with the risk of endometrial cancer in subgroup analysis. We found that age exacerbated the increased risk of SNP rs7128029-related endometrial cancer risk, especially for those aged >61 (**Fig. 1**). Moreover, the risk of endometrial cancer associated with the SNP rs7128029 was significantly exacerbated among patients that smoked (**Fig. 1**).

Table 2. Association between AA/GG genotype and susceptibility to endometrial cancer in the crude analysis and propensity-score analyses

Analysis	Cases or controls
No. of events/No. of patients at risk (%)	
AA	1,326/1,425 (93.05)
GG	93/70 (132.86)
Multivariable analysis	1.428 (1.038–1.964)
Propensity-score analyses	
With matching	1.666 (1.194–2.324)
Inverse probability weighting analyses	1.006 (0.803–1.260)

Values are presented as number (%) or odds ratio (95% confidence interval).
Adjusted for age, smoking status, drinking status

Table 3. Association analyses between individual SNP and endometrial cancer risk in the 2 phases and combined samples

Genetic model	Genotypes	Cases (n=2,000)	Controls (n=2,013)	Adjust OR (95% CI)	p
		No. (%)	No. (%)		
Additive model	AA	1,326 (66.3)	1,425 (70.8)	1	
	AG	581 (29.0)	518 (25.7)	1.205 (1.048–1.387)	0.009
	GG	93 (4.6)	70 (3.5)	1.428 (1.038–1.964)	0.028
Dominant model	AA	1,326 (66.3)	1,425 (70.8)	1	
	AG/GG	674 (33.7)	588 (29.2)	1.232 (1.078–1.408)	0.002
Recessive model	AA/AG	1,907 (95.4)	1,943 (96.5)	1	
	GG	93 (4.6)	70 (3.5)	1.354 (0.986–1.858)	0.060

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Variables	Cases		Controls		Adjust OR (95% CI)	p
	AA	AG/GG	AA	AG/GG		
	No. (%)	No. (%)	No. (%)	No. (%)		
Age (yr)						
≤50	317 (96.6)	11 (3.4)	286 (85.6)	48 (14.4)	0.207 (0.105–0.406)	<0.001
51–60	455 (80.2)	112 (19.8)	435 (78.2)	121 (21.8)	0.885 (0.663–1.181)	0.407
61–70	426 (56.1)	333 (43.9)	538 (67.8)	256 (32.2)	1.643 (1.336–2.020)	<0.001
≥71	128 (37.0)	218 (63.0)	166 (50.5)	163 (49.5)	1.734 (1.276–2.358)	<0.001
Smoking						
No	1,326 (69.3)	587 (30.7)	1,409 (72.9)	525 (27.1)	1.188 (1.033–1.366)	0.016
Yes	0 (0.0)	87 (100.0)	16 (20.3)	63 (79.7)	2.338 (1.946–2.811)	0.008
Drinking						
No	996 (64.1)	558 (35.9)	1,190 (76.1)	374 (23.9)	1.783 (1.526–2.083)	<0.001
Yes	330 (74.0)	116 (26.0)	235 (52.3)	214 (47.7)	0.386 (0.291–0.511)	<0.001

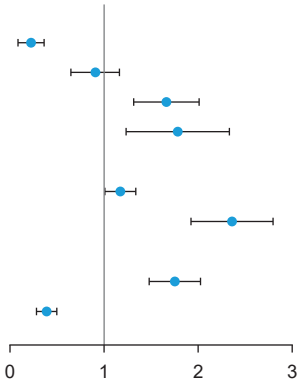

Fig. 1. Stratified analysis of the association between SNP rs7128029 and endometrial cancer.
CI, confidence interval; OR, odds ratio; SNP, single nucleotide polymorphism.

3. Splicing quantitative trait loci analysis

We obtained endometrial cancer splicing data, including 92,641 splicing pairs, 25,833 sQTL, and 372 splicing events, from the CancerSplicingQTL. The endometrial cancer splicing data showed that SNP rs7128029 controls the splicing ratio of exon 2 in *PSMD13* in an exon-skipping manner. When the SNP rs7128029 allele was mutated from A to G, the expression level of exon 2 of *PSMD13* was markedly decreased (p<0.001) (**Fig. 2**). Splicing function prediction tools such as SPANR and Spliceman2 exhibited results which consistent with our findings. The decreased expression of exon 2 of *PSMD13* generated by SNP rs7128029, which reduces locus activity and inhibits exon recognition, consequently promoting exon skipping (**Table S5**). Therefore, SNP rs7128029 G>A functions as an alternative splicing regulator and implicated in the etiology of endometrial cancer.

4. Effect of PSMD13 on survival of patients with endometrial cancer

We further explored the association of *PSMD13* expression with various clinical indicators (age, pathological tumor-node-metastasis stage, grade, and status) in patients with endometrial cancer using TCGA. These results are presented using the Sankey diagram, showing that patients with high *PSMD13* expression had a higher survival rate (**Fig. 3A**). Furthermore, K-M Plotter website and The Human Protein Atlas was used to explore the effect of *PSMD13* expression on the survival of patients with endometrial cancer. The results showed that overall survival is longer in patients with higher *PSMD13* expression than in those with low *PSMD13* levels (p=3.13e-31, p=3.90e-31, and p<0.001, respectively) (**Fig. 3B-D**).

DISCUSSION

Endometrial cancer is one of the most common gynecological malignancies, and its incidence is increasing every year due to an aging population [5]. Despite enormous advances in pharmacological and surgical treatments have been achieved, however the early screening and survival of patients with endometrial cancer remain an urgent issue [22]. Considering that the inherited germline variant functions as a crucial component in the etiology of endometrial cancer [23]. Therefore, understanding and identifying the genetic variants involved in the mechanisms of endometrial cancer is essential for gaining insight

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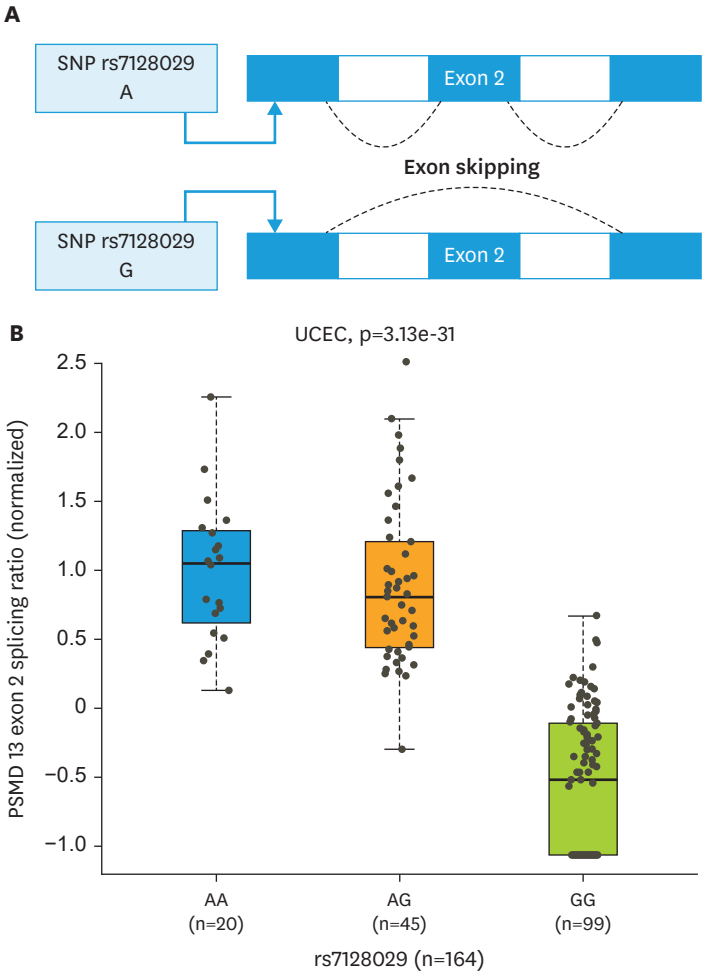

Fig. 2. Alternative splicing of SNP rs7128029.
(A) Exon 2 jumping due to the SNP rs7128029 mutation. (B) The correlation between SNP rs7128029 and the splicing events of *PSMD13* in endometrial cancer was evaluated through CancerSplicingQTL database.
SNP, single nucleotide polymorphism.

into the etiology and developing specific biomarkers for early screening of endometrial cancer. Alternative splicing is strongly associated with the development, progression, and metastasis including endometrial cancer [24,25]. Therefore, uncovering the genetic variation that controls the alternative splicing events is closely associated with endometrial cancer susceptibility could deepen our understanding of the underlying molecular events of endometrial cancer. Initially, we revealed that the SNP rs7128029 was related to the alternative splicing in endometrial cancer from the CancerSplicingQTL database. Furthermore, the association between SNP rs7128029 with endometrial cancer susceptibility was verified by large-scale case-control study. Our integrated epidemiological data with CancerSplicingQTL database analysis contributes to uncovering variants-related alternative splicing with the risk of endometrial cancer.

Cumulative evidence indicates that functional SNPs are closely linked to the risk of endometrial cancer through disturbing the biological functions and directional or post-transcriptional regulation of the expression of targeted genes [11,26,27]. In our study, we concluded from 2,026 endometrial cancer cases and 2,020 control cases genomic analyses

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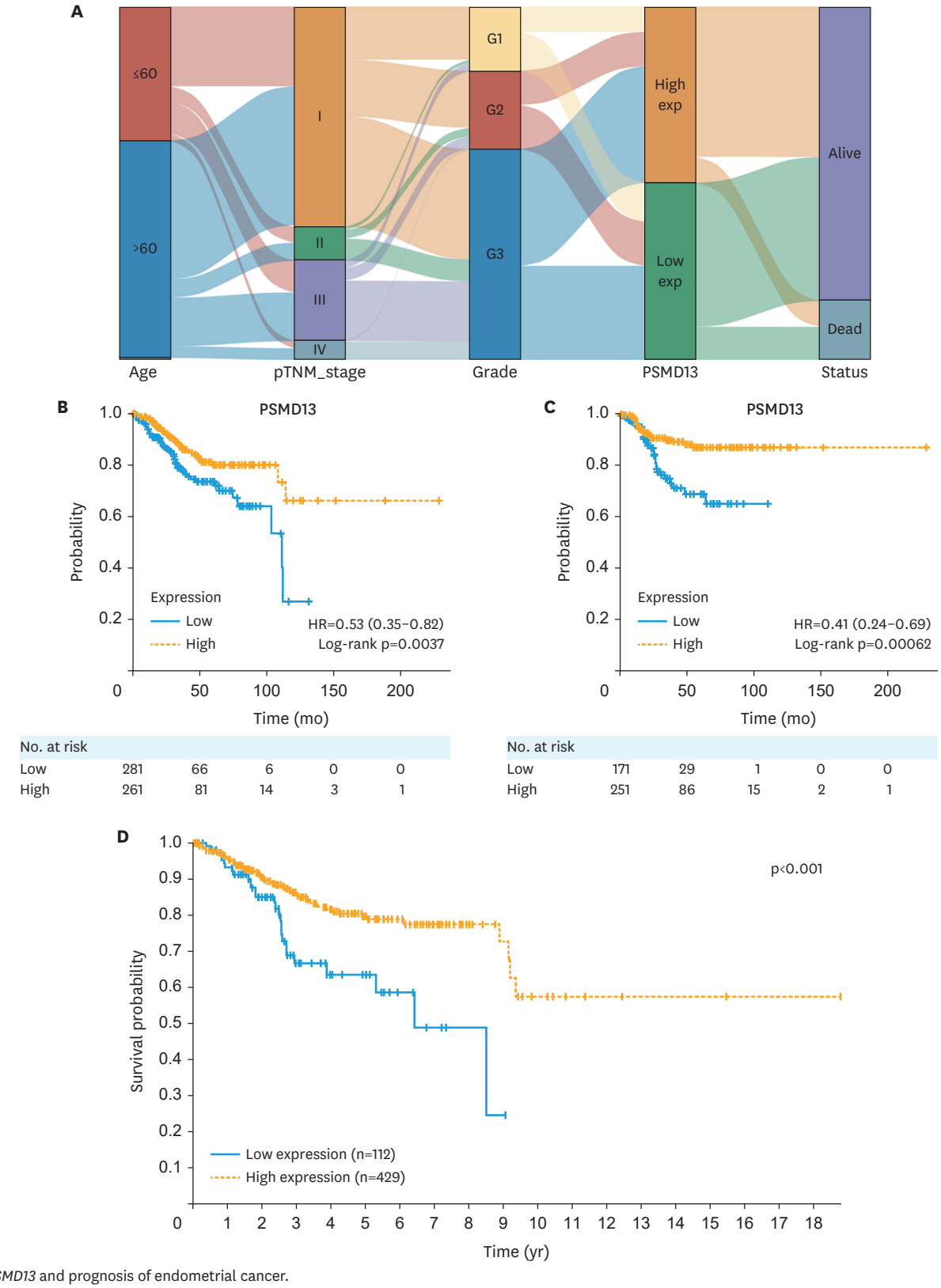

Fig. 3. *PSMD13* and prognosis of endometrial cancer.
(A) *PSMD13* in endometrial cancer samples with different stages, age and other clinical characteristics and patient survival, the distribution trend of high and low gene expression. (B) The influence of *PSMD13* expression on the prognosis of endometrial cancer patients through K-M Plotter (overall survival). (C) The influence of *PSMD13* expression on the prognosis of endometrial cancer patients through K-M Plotter (relapse-free survival). (D) The influence of *PSMD13* expression on the prognosis of endometrial cancer patients through The Human Protein Atlas.
K-M, Kaplan-Meier.

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of CancerSplicingQTL integrated with epidemiological data revealed that SNP rs7128029 G>A increased the risk of endometrial cancer. However, whether SNP rs7128029 G>A affects the initiation and development of endometrial cancer are remain unclear. In the subgroup analysis, the association of SNP rs7128029 G>A with an increased risk of endometrial cancer was more pronounced among older populations in an apparent age-dependent manner. Considering that age is a substantial risk factor for endometrial cancer, therefore, SNP rs7128029 G>A could synergize with age to exacerbate the increased risk of endometrial cancer [28]. In addition, unhealthy lifestyle presents another risk factors for increasing the predisposition to endometrial cancer [29]. Consistently, we found that the rs7128029 G>A-endometrial cancer association was more pronounced in the population who are smoker.

The Human Genome Project and the improvement of gene sequencing technology allow genetic targets for many diseases could be identified through gene sequencing and gene database matching [30]. Several molecular and genetic events have been observed during the development of endometrial cancer, which enable us to better understand the biological events during the development of endometrial disease [31]. Alternative splicing is a vital post-transcriptional regulatory mechanism that implicates the development and progression of a wide spectrum of cancers [15]. Aberrant modification of the splicing site or functional element located on pre-RNA could dysregulate biological functions and produce pro-carcinogenic proteins. Cumulative evidence has revealed that cancer-associated genetic variants or mutations impact endometrial cancer susceptibility by regulating pre-mRNA alternative splicing [32]. In our study, SNP rs7128029-related pre-mRNA splicing of *PSMD13* was markedly associated with an increased risk of endometrial cancer. *PSMD13* functions as a component of the 26S proteasome, a multi-protein complex involved in the ATP-dependent degradation of ubiquitinated proteins. This multi-protein complex plays a key role in maintaining proteostasis by eliminating misfolded or damaged proteins and loss-of-function proteins, which may impair cellular function [33]. We speculate that this may be due to the rs7128029 variant affecting the structure of a proteasome via pre-mRNA splicing to influence apoptosis of cancer cells, thereby decreasing apoptosis of endometrial cancer cells and thus increasing the risk of endometrial cancer infection. Therefore, *PSMD13*, identified in this study, might affects the risk of endometrial cancer by regulating the protease-mediated cell cycle, but this requires further in vivo and in vitro experimental validation. Furthermore, considering that aberrant alternative of key gene that implicated in the pathogenesis of cancer, that is oncogene splicing could decrease its expression and finally resulting the occurrence of cancer [34]. Therefore, we reasoned that rs7128029 locates in *PSMD13* might decrease the expression of *PSMD13* through regulating the exon 2 skipping, which contribute to increased risk of endometrial cancer. But the above speculation also needs to be further validated in endometrial cancer tissue.

Our study systematically dissected the role of SNP-related alternative splicing on the risk of endometrial cancer by integrating epidemiological data with CancerSplicingQTL database. However, there are still shortcomings in this study that need to be improved: 1) endometrial cancer is a multifactorial disease, and the effects of smoking, alcohol consumption, diet, and lifestyle habits have all been reported to increase susceptibility. However, the data on behavioral factors collected in this study was limited, and only data on smoking and alcohol consumption were collected, which needs to be improved in a follow-up study, and a comprehensive analysis is required to construct a model of gene-environment interaction in endometrial cancer. In addition, the modifiable effect of pathological data on the rs7128029 G>A or alternative splicing events-endometrial cancer association needs to be considered.

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Furthermore, the prognosis of rs7128029 G>A or alternative splicing events on the incidence of endometrial cancer is also another forward question. 2) TCGA data collected in this study contained mostly non-Asian samples, and there is currently no comparable data available in China; therefore, further experiments are needed to obtain information on sQTL annotations for endometrial cancer in the Chinese population. 3) This study preliminarily investigated the effect of alternative splicing due to genetic variation on cancer risk, and there is a lack of large data to support the pre-variable splicing selection, which will be further validated by cell and animal experiments in future studies.

Taken together, we uncovered that the rs7128029-related AS event of *PSMD13* is associated with risk of endometrial cancer by integrating CancerSplicingQTL and large-scale population data. Moreover, the gene map of endometrial cancer susceptibility was improved, and genetic variant-associated alternative splicing event of *PSMD13* was suggested to be an early detection or diagnostic marker for endometrial cancer. At present, early screening of endometrial cancer in clinical practice usually relies on hormone levels, without early screening markers for endometrial cancer [35]. The results of this study provide new clues to the pathogenesis of endometrial cancer. The study has important implications for the early screening of Chinese people at high risk of endometrial cancer.

ACKNOWLEDGEMENTS

We wish to thank all the patients who indirectly participated in this study.

SUPPLEMENTARY MATERIALS

Table S1
The characteristics of the endometrial cancer cases and healthy controls (after PSM)

Click here to view

Table S2
The characteristics of the endometrial cancer cases and healthy controls (after IPTW)

Click here to view

Table S3
Splicing events of the top 10 significant SNPs involved in endometrial cancer risk

Click here to view

Table S4
Splicing events of the top 7 significant SNPs involved in gene *PSMD13*

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Table S5
Candidate mutation rs7128029 splicing function prediction result

Click here to view

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