

High *SLC20A1* Expression Indicates Poor Prognosis in Prostate Cancer

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Abstract. *Background/Aim:* High expression of solute carrier family 20 member 1 (*SLC20A1*) indicates poor clinical outcomes for patients with breast cancer subtypes treated with endocrine therapy and radiotherapy. However, the association between *SLC20A1* expression and clinical outcomes in prostate cancer remains to be determined. *Materials and Methods:* Open-source datasets (The Cancer Genome Atlas prostate, Stand Up to Cancer-Prostate Cancer Foundation Dream Team, and The Cancer Genome Atlas PanCancer Atlas) were downloaded and analyzed. *SLC20A1* expression was analyzed in prostate cancer and normal prostate tissue. Survival analysis using Kaplan–Meier curves and Cox

regression analysis were performed to examine patient prognosis, as well as the effects of endocrine therapy and radiotherapy on high *SLC20A1* expression in patients with prostate cancer. *Results:* *SLC20A1* was higher in prostate cancer than in normal prostate tissues. High *SLC20A1* expression predicted poor disease-free and progression-free survival. Following endocrine therapy, no significant difference in prognosis was observed between patients with high *SLC20A1* and those with low *SLC20A1* expression. However, following radiotherapy, high *SLC20A1* expression tended to be associated with a poor clinical outcome. *Conclusion:* *SLC20A1* may serve as a prognostic biomarker for prostate cancer, and the recommended treatment for patients with high *SLC20A1* expression is endocrine therapy.

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Key Words: Prostate cancer, *SLC20A1*, prognostic marker.

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Prostate cancer was the most frequently diagnosed type of cancer among men in 112/185 of the countries in the world in 2020 (1). Active surveillance, endocrine therapy, radiotherapy and surgery are all treatments for prostate cancer (2). However, radiotherapy, endocrine therapy and surgery are not the primary treatment options, as they have serious side-effects and can reduce the quality of life (QOL) of patients. Furthermore, patients with low-risk, localized prostate cancer often receive unnecessary radiotherapy, endocrine therapy and surgery. To overcome this problem leading to reduced QOL, recently, active surveillance has

been recommended for primary treatment (3). Active surveillance is the monitoring of low-risk localized prostate cancer progression by prostate-specific antigen (PSA) testing and biopsy. Patients treated with active surveillance are monitored until the prostate cancer grows to a point where it can receive active treatments such as endocrine therapy, radiotherapy and surgery. Thus, patients can have a normal life without their QOL being reduced.

The PSA test is an established diagnostic method used for prostate cancer detection and monitoring of cancer recurrence following active treatment (4). However, the PSA test alone is not sufficient for prediction of prognosis, as biopsy-based biomarkers and surgical specimens remain important. Furthermore, as active treatments, such as endocrine and radiation therapy can reduce the patients' QOL, it is important to determine the appropriate treatment for each patient. Therefore, in order to accurately predict prostate cancer prognosis, the identification of novel biomarkers is required.

Solute carrier family 20 member 1 (*SLC20A1*) is a gene that encodes a sodium/phosphate symporter (5, 6) and has been proposed to be a viable prognostic marker for breast, tongue and pancreatic cancer (7-10). Previous data showed that high *SLC20A1* expression also indicates poor clinical outcomes for patients with breast cancer subtypes which are treated with endocrine therapy and radiotherapy (11, 12). In addition, high *SLC20A1* expression can predict the late recurrence of estrogen receptor (ER) positive-breast cancer treated with endocrine therapy or radiotherapy (11, 12). A series of loss-of-function studies have revealed that *SLC20A1* is involved in the promotion of the cell cycle progression of HeLa cells, in the viability of HeLa, HepG2, MCF-7, MDA-MB231 and MDA-MB468 cells and in the suppression of tumor necrosis factor-induced apoptosis of HeLa cells (8, 13, 14). Furthermore, *SLC20A1* is involved in the viability and tumor-sphere formation of by aldehyde dehydrogenase 1 (ALDH1)-positive breast cancer stem cells (8). However, the association between *SLC20A1* gene expression and the clinical outcomes of endocrine therapy and radiotherapy in prostate cancer remains to be determined.

Materials and Methods

Analysis of The Cancer Genome Atlas (TCGA) prostate cancer dataset. TCGA prostate cancer dataset (15, 16) was downloaded from the University of California, Santa Cruz (UCSC) Xena cancer genomics visualization tools (<https://xena.ucsc.edu>) (17) on November 7, 2022. This dataset contained mRNA expression data from 52 samples of normal solid tissue and 497 primary prostate tumor samples. The mRNA expression of *SLC20A1* was present in both normal and cancer tissues, and was converted to a z-score, and box and bee swarm plots were made.

Analysis of the stand Up to Cancer (SU2C)-Prostate Cancer Foundation (PCF) Dream Team. The SU2C-PCF Dream Team prostate cancer dataset (18) was downloaded from cBioPortal

(<https://www.cbioportal.org/>) (19, 20) on October 26, 2022. This dataset contained a total of 208 mRNA expression data from 444 prostate cancer samples. Of these, 71 samples had OS data along with mRNA expression data; the clinicopathological data of these patients are summarized in Table I. The mRNA expression of *SLC20A1* was presented using the log₂ median-centered ratio for cancer tissues.

Analysis of TCGA, PanCancer Atlas dataset. The PanCancer Atlas dataset (n=184) (15, 16) was downloaded from cBioPortal (<https://www.cbioportal.org/>) (19, 20) on October 26, 2022. The clinicopathological data from these patients are also summarized in Table I. The PanCancer Atlas dataset contained data on both gene alterations (n=494) and mRNA expression levels in primary prostate cancer samples (n=493), and overall survival (OS), disease-specific survival (DSS), disease-free survival (DFS) and progression-free survival (PFS) data according to mRNA expression levels. Patients treated with endocrine therapy were categorized as patients whose treatment type was endocrine therapy and patients without endocrine therapy were categorized as patients whose treatment type was chemotherapy or radiation therapy; patients were categorized as being treated with radiotherapy or not.

Statistical analysis. *SLC20A1* mRNA expression was compared between normal solid tissue and primary tumor tissue with box plot and bee swarms using the Mann–Whitney *U*-test; a two-sided value of $p < 0.05$ was considered to indicate a statistically significant difference. *SLC20A1* mRNA expression was compared among tissue sites with box plots using the Kruskal–Wallis test with the Steel–Dwass test; a value of $p < 0.05$ was considered to indicate a statistically significant difference. Cut-off values for dividing the patients into groups with high and low *SLC20A1* expression were determined by Youden's index using receiver operating characteristic curves (Table II). The Kaplan–Meier method was used to analyze the survival curves of OS, DSS, DFS and PFS. For the survival curves, the log-rank (Cochran–Mantel–Haenszel) tests were used to calculate *p*-values. In order to evaluate the influence of *SLC20A1* on prognosis, Cox regression analysis was used to estimate the adjusted hazard ratios (HRs), 95% confidence intervals and *p*-values, with age at diagnosis in the model as a confounding factor. Cut-off values, Kaplan–Meier curves, and Cox regression analysis were performed using Bell-Curve for Excel version 4.02 (Social Survey Research Information Co., Ltd., Tokyo, Japan). Fisher's exact and chi-squared tests were used to test for correlations of clinical and pathological factors the high and low *SLC20A1* expression; their *p*-values were calculated by two-sided hypotheses using Excel version 4.02 (Social Survey Research Information Co., Ltd., Tokyo, Japan) and R version 4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

SLC20A1 expression is higher in prostate cancer than in normal prostate tissue. To examine *SLC20A1* expression in primary prostate cancer and normal prostate tissue from the same patients, TCGA prostate dataset containing data from 549 patients was analyzed. *SLC20A1* expression was found to be higher in primary prostate cancer than in normal

Table I. Clinicopathological data from the Stand Up To Cancer-Prostate Cancer Foundation Dream Team (SU2C/PCF) prostate cancer and The Cancer Genome Atlas PanCancer Atlas (TCGA) datasets.

Dataset	Factor	Subgroup	Value		
SU2C/PCF	Age, years	Mean (range)	61.5 (41.6-75.9)		
		Tissue site, n (%)	Prostate 5 (1.1%) LN 79 (17.8%) Bone 82 (18.5%) Liver 26 (5.9%) Adrenal gland 2 (0.5%) Other soft tissue 14 (3.2%) NA 236 (53.2%)		
	Gleason score, n (%)	≤6	29 (6.5%)		
		7	107 (24.1%)		
		≥8	222 (50.0%)		
	OS	Status, n (%)	NA	86 (19.4%)	
			Living Deceased NA	26 (5.9%) 45 (10.1%) 373 (84.0%)	
	TCGA	Age, years	Duration, months	Median (range) 19.1 (1.7-69.0)	
			OS	Status, n (%)	Mean (range) 61.0 (41.0-78.0) Living 483 (98.0%) Deceased 10 (2.0%) NA 0 (0.0%)
		DSS	Status, n (%)	Duration, months	Median (range) 30.4 (0.8-165.2)
				Tumor-free, alive or dead Dead with tumor NA	486 (98.6%) 5 (1.0%) 2 (0.4%)
DFS		Status, n (%)	Duration, months	Median (range) 30.4 (0.8-165.2)	
			Disease-free Recurrence/progression NA	303 (61.5%) 30 (6.1%) 160 (32.5%)	
PFS		Status, n (%)	Duration, months	Median (range) 30.3 (1.9-165.2)	
			Censored Progression NA	400 (81.1%) 93 (18.9%) 0 (0.0%)	
pN Stage, n (%)		Duration, months	Median (range)	25.7 (0.8-165.2)	
			N1 N0 NA	78 (15.8%) 342 (69.4%) 73 (14.8%)	
pT Stage, n (%)		Duration, months	T2A	13 (2.6%)	
	T2B		10 (2.0%)		
	T2C		163 (33.1%)		
	T3A		157 (31.8%)		
	T3B		133 (27.0%)		
	T4		10 (2.0%)		
	NA		7 (1.4%)		
	Endocrine therapy, n (%)		No Yes NA	37 (7.5%) 71 (14.4%) 385 (78.1%)	
Radiation therapy, n (%)	No Yes NA	388 (78.7%) 59 (12.0%) 46 (9.3%)			

DFS: Disease-free survival; DSS: disease-specific survival; OS: overall survival; PFS: progression-free survival.

prostate tissue (Figure 1A). *SLC20A1* mutations detected included missense (0.5%; 2/444, SU2C-PCF Dream Team dataset) and deletions (0.2%; 1/494, TCGA PanCancer Atlas dataset). Other gene alterations, including gene amplification

and fusion, were not detected. No significant differences in *SLC20A1* expression were observed between primary prostate cancer and metastases such as lung, bone, liver and other soft tissue (Figure 1B).

Table II. The cut-off value determined by Youden's index using receiver operating characteristic curves for survival endpoints for the Stand Up To Cancer-Prostate Cancer Foundation Dream Team (SU2C/PCF) prostate cancer and The Cancer Genome Atlas PanCancer Atlas (TCGA) datasets.

Dataset	Patient group		Endpoint	Cut-off value
SU2C/PCF	All		OS	-0.9658
TCGA	All		OS	0.0866
			DSS	0.1421
			DFS	0.0333
			PFS	0.0159
	Endocrine therapy	Without	OS	0.2233
			DSS	0.2233
			DFS	0.3470
		With	PFS	0.1571
			OS	0.7017
			DSS	0.7017
	Radiotherapy	Without	DFS	2.5184
			PFS	1.0918
			OS	-0.8074
		With	DSS	-0.5146
			DFS	-0.1367
			PFS	0.0159
			OS	0.2233
			DSS	0.2233
		DFS	0.0932	
		PFS	0.0932	

DFS: Disease-free survival; DSS: disease-specific survival; OS: overall survival; PFS: progression-free survival.

Next, the association between *SLC20A1* expression and clinicopathological data, including Gleason score and PSA level, was examined by Pearson's chi-square and Fisher's exact tests. *SLC20A1* expression was associated with N and T categories (Table III). It was also shown that neither Gleason score nor PSA level were significantly correlated with *SLC20A1* expression.

High expression of SLC20A1 indicates poor DSS, DFS and PFS in patients with prostate cancer. To examine the association between *SLC20A1* expression and the clinical outcomes of prostate cancer, the SU2C-PCF Dream Team and TCGA PanCancer Atlas datasets were downloaded and OS was analyzed according to *SLC20A1* expression status. The results of Kaplan–Meier and Cox regression analyses showed no significant difference in OS between *SLC20A1*^{high} and *SLC20A1*^{low} groups (Figure 1C and D, and Table IV). Since the SU2C-PCF Dream Team dataset contained only OS data, differences in DSS, DFS and PFS between the *SLC20A1*^{high} and *SLC20A1*^{low} groups were analyzed using TCGA PanCancer Atlas dataset (Figure 1D and Table IV). It was discovered that *SLC20A1*^{high} status was associated with poor DSS, DFS and PFS ($p < 0.05$). Cox regression analysis for DSS, DFS and PFS was also performed and showed high *SLC20A1* expression to be significantly associated with poor DFS and PFS; HRs were 2.97 and 2.66, respectively (Table IV). These results suggest that high *SLC20A1* expression is associated

with poor prognosis, and that it is involved in and contributes to prostate cancer recurrence and progression.

Endocrine therapy is effective for SLC20A1^{high} prostate cancer. Our previous study showed that endocrine therapy is not effective for *SLC20A1*^{high} breast cancer (11). We therefore analyzed whether endocrine therapy was effective for patients with *SLC20A1*^{high} prostate cancer (Figure 2A and Table IV). The Kaplan–Meier curves for OS, DSS, DFS and PFS revealed no significant differences between the *SLC20A1*^{high} and *SLC20A1*^{low} groups in patients with and without endocrine therapy (Figure 2A). Cox regression analysis was also used to study the effects of *SLC20A1* expression on OS, DSS, DFS and PFS; it was not possible to analyze OS and DSS in the patients without endocrine therapy (Table IV). Cox regression analysis revealed no significant differences in the effects of *SLC20A1* expression on the prognosis of patients with or without endocrine therapy ($p > 0.05$; Table IV). Collectively, these results suggested that endocrine therapy is effective for *SLC20A1*^{high} prostate cancer, unlike breast cancer.

Patients with SLC20A1^{high} prostate cancer treated with radiotherapy tend to have poor clinical outcomes. Our previous study showed that radiotherapy is not effective for *SLC20A1*^{high} breast cancer (12). Therefore, the prognosis of patients with and without radiotherapy was next compared by

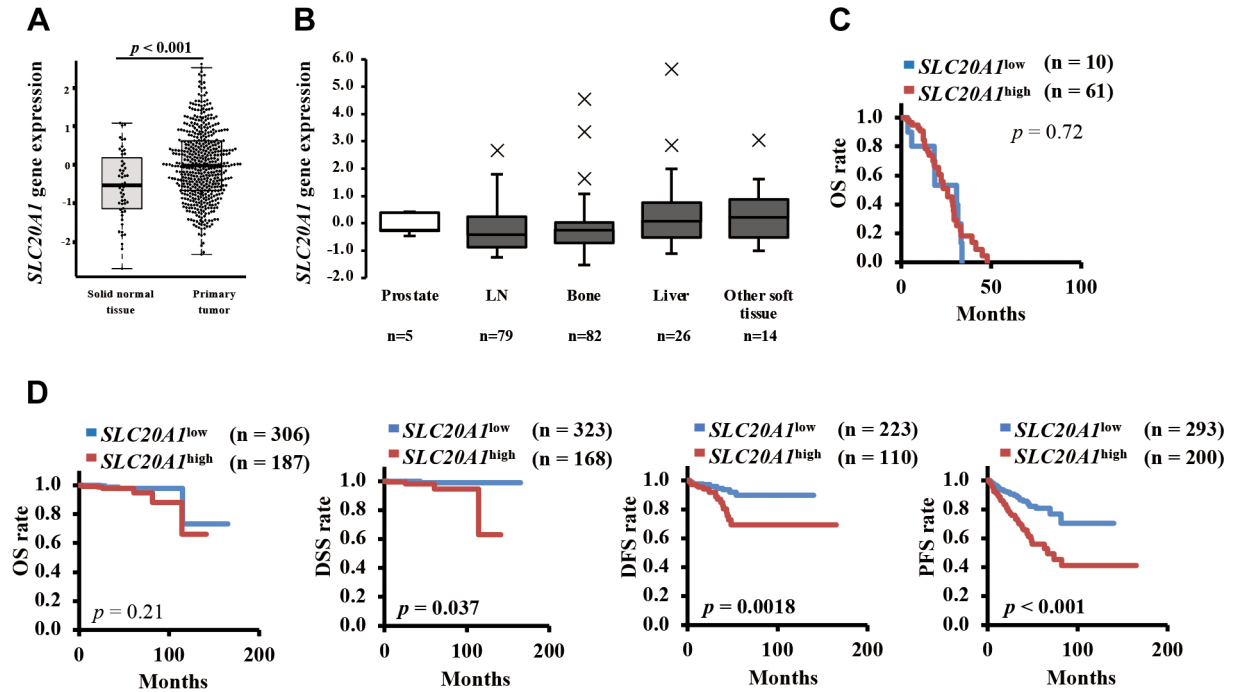


Figure 1. Expression of solute carrier family 20 member 1 (*SLC20A1*) mRNA in solid normal tissue, primary tumors and other cancer sites and survival according to *SLC20A1* mRNA expression: A: Box and bee swarm plots showing *SLC20A1* mRNA levels in solid normal tissue (n=52) and primary tumors (n=497) in The Cancer Genome Atlas prostate cancer datasets downloaded from UCSC Xena. p-Value is from two-sided Mann–Whitney U-test. B: Box plot showing *SLC20A1* mRNA levels in prostate and other tissues using the Stand Up To Cancer-Prostate Cancer Foundation Dream Team prostate cancer dataset. Kruskal–Wallis with Steel–Dwass test showed no significant differences between tissues. C: Kaplan–Meier analysis comparing overall survival (OS) between the *SLC20A1*^{high} and *SLC20A1*^{low} groups of patients from the SU2C-PCF Dream Team prostate cancer dataset. D: Kaplan–Meier analysis comparing OS, disease-specific (DSS), disease-free (DFS) and progression-free (PFS) survival, respectively, between the *SLC20A1*^{high} and *SLC20A1*^{low} groups of patients using The Cancer Genome Atlas PanCancer Atlas datasets. High expression of *SLC20A1* was associated with poor DSS, DFS and PFS in patients with prostate cancer.

Table III. Association between clinicopathologic parameters and solute carrier family 20 member 1 (*SLC20A1*) mRNA expression using Stand Up To Cancer-Prostate Cancer Foundation Dream Team (SU2C/PCF) and The Cancer Genome Atlas PanCancer Atlas (TCGA) data.

Factor	Dataset		Frequency, n (%)		p-Value
			<i>SLC20A1</i> ^{high}	<i>SLC20A1</i> ^{low}	
Age, years	SU2C/PCF	≥61.5 Years	30 (6.8%)	5 (1.1%)	0.45 ^b
		<61.5 Years	26 (5.9%)	2 (0.5%)	
	TCGA	≥61.0 Years	98 (19.9%)	172 (34.9%)	0.28 ^a
		<61.0 Years	70 (14.2%)	151 (30.6%)	
Gleason score	SU2C/PCF	High (≥8)	29 (6.5%)	4 (0.8%)	0.71 ^b
		Middle (7)	19 (3.9%)	1 (0.2%)	
		Low (≤6)	7 (1.4%)	1 (0.2%)	
PSA	SU2C/PCF	High (≥20 ng/ml)	31 (6.3%)	3 (0.6%)	0.42 ^b
		Middle (≥10-<20 ng/ml)	6 (1.2%)	1 (0.2%)	
		Low (<10 ng/ml)	24 (4.9%)	6 (1.2%)	
pN Stage	TCGA	N0	108 (21.9%)	233 (47.3%)	0.001^a
		N1	41 (8.3%)	36 (7.3%)	
pT Stage	TCGA	T2A	5 (1.0%)	8 (1.6%)	0.001^b
		T2B or T2C	40 (8.1%)	133 (27.0%)	
		≥T3A	121 (24.5%)	177 (35.9%)	

pN/pT: Pathological N/T; PSA: Prostate-specific antigen. ^aChi-squared test, ^bFisher’s exact test. Significant differences are shown in bold.

Table IV. Multivariate Cox regression analysis of overall (OS), disease-specific (DSS), disease-free (DFS) and progression-free (PFS) survival in patients with and without endocrine therapy and radiotherapy. The hazard ratio (HR) for the group with high expression of solute carrier family 20 member 1 (*SLC20A1^{high}*) was compared with the *SLC20A1^{low}* group adjusted using age as a confounding factor, as estimated using a Cox proportional hazards model for data from the Stand Up To Cancer-Prostate Cancer Foundation Dream Team (SU2C/PCF) and The Cancer Genome Atlas PanCancer Atlas (TCGA) datasets.

Dataset			Endpoint	HR	95% CI	p-Value
SU2C/PCF			OS	0.81	0.36-1.81	0.61
TCGA			OS	2.23	0.62-7.99	0.22
			DSS	6.80	0.75-61.30	0.087
			DFS	2.97	1.43-6.18	0.0035
			PFS	2.66	1.75-4.04	<0.001
			OS	1.82	0.12-26.64	0.66
TCGA	Endocrine therapy	With	DSS	1.82	0.12-26.64	0.66
		Without	DFS	1.18	0.19-7.18	0.86
		With		0.49	0.055-4.31	0.52
		Without	PFS	1.98	0.71-5.53	0.19
		With		0.79	0.37-1.70	0.55
		Without	OS	1.14	0.20-6.58	0.88
	Radiotherapy	Without	DFS	2.88	1.21-6.88	0.017
		With		1.58	0.26-9.82	0.62
		Without	PFS	2.51	1.57-4.00	<0.001
		With		3.21	0.90-11.39	0.071

CI: Confidence interval; DFS: disease-free survival; DSS: disease-specific survival; OS: overall survival; PFS: progression-free survival. Significant differences are shown in bold. Note that it was not possible to analyze DSS for patients treated without radiotherapy or OS and DSS for those treated with radiotherapy, nor OS and DSS in patients without endocrine therapy.

SLC20A1 expression status (Figure 2B and Table IV). The Kaplan–Meier curves for OS and DSS indicate that there were no significant differences according to *SLC20A1* expression status in patients treated with and without radiotherapy. The Kaplan–Meier curves for DFS and PFS in the patients treated without radiotherapy indicate that patients of the *SLC20A1^{high}* group had a poorer prognosis than those of the *SLC20A1^{low}* group (Figure 2B). On the other hand, the curves for DFS and PFS in patients treated with radiotherapy revealed no statistically significant difference between *SLC20A1^{high}* and *SLC20A1^{low}* groups. However, DFS and PFS of patients with *SLC20A1^{high}* prostate cancer treated with radiotherapy showed a tendency towards poorer prognosis (Figure 2B), which suggests that radiotherapy is not sufficient for reducing the recurrence and progression of *SLC20A1^{high}* prostate cancer. Cox regression analysis was performed to investigate the effects of *SLC20A1* on the prognosis of patients treated with and without radiotherapy (Table IV); it was not possible to analyze DSS for the patients treated without radiotherapy, nor OS and DSS for those treated with radiotherapy. Only the DFS and PFS of the patients without radiotherapy were significant ($p < 0.05$; Table IV). The HRs of patients with prostate cancer treated without radiotherapy were 2.88 for DFS and 2.51 for PFS. Of note, although the Kaplan–Meier curves and Cox regression analysis results revealed no differences between *SLC20A1^{high}* and *SLC20A1^{low}* groups treated with radiotherapy, the survival rate of patients in the *SLC20A1^{high}*

group was lower than that of those in the *SLC20A1^{low}* group at all time points. Therefore, these results suggest that patients with *SLC20A1^{high}* prostate cancer treated with radiotherapy tend to have poor clinical outcomes.

Discussion

In the present study, *SLC20A1* expression in prostate cancer was found to be higher than that of normal prostate tissue (Figure 1A). This is consistent with the result of previous study showing that *SLC20A1* is overexpressed in breast cancer (8). Consistent with the findings of the same study on breast cancer, *SLC20A1* mutation was also detected at a very low frequency in prostate cancer. Thus, a high *SLC20A1* expression in prostate cancer may be associated with transcriptional regulation. Consistent with the findings of previous studies on breast, pancreatic and tongue cancer (8–11), *SLC20A1^{high}* prostate cancer was associated with poor DSS. In addition, *SLC20A1^{high}* prostate cancer was associated with poor DFS and PFS. Furthermore, *SLC20A1* was similarly expressed among prostate, lymph node, bone, liver and other soft tissue in patients with prostate cancer (Figure 1B). Our previous studies showed that patients with *SLC20A1^{high}* breast cancer had a high recurrence rate, suggesting metastasis (8, 11). *SLC20A1* is involved in the promotion of the cell cycle, cell viability, and tumor-sphere formation, and the suppression of apoptosis, in HeLa cells, HepG2 cells and certain breast

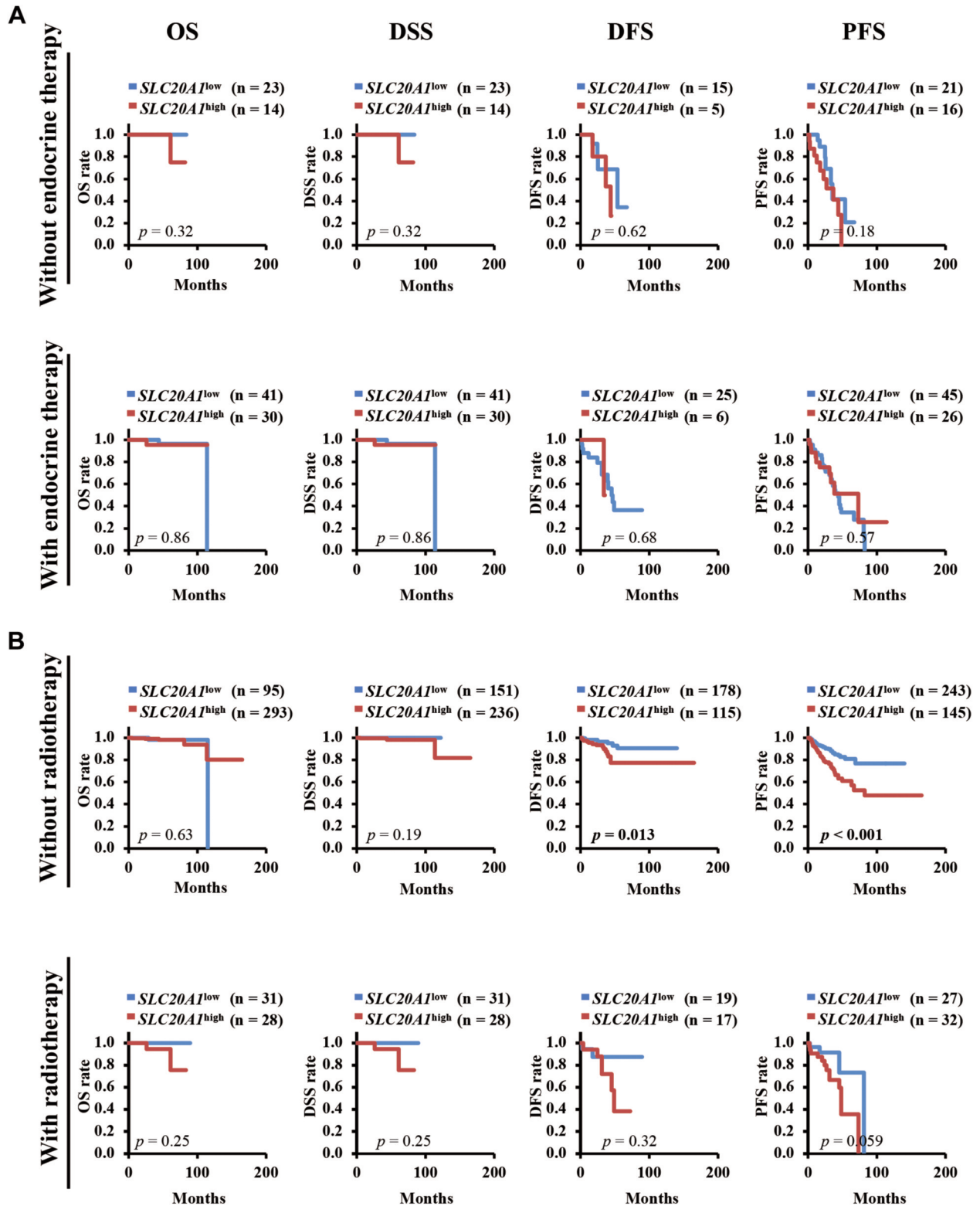


Figure 2. Patients with high mRNA expression of solute carrier family 20 member 1 (*SLC20A1*^{high}) treated with radiotherapy have a tendency for poor clinical outcomes. Kaplan–Meier analyses comparing overall (OS), disease-specific (DSS), disease-free (DFS) and progression-free (PFS) survival, respectively, between the *SLC20A1*^{high} and *SLC20A1*^{low} groups of patients treated with and without endocrine therapy (A) and with or without radiotherapy (B) using The Cancer Genome Atlas PanCancer Atlas datasets.

cancer cell lines (8, 13, 14). Our findings suggested that high *SLC20A1* expression may similarly be involved in cancer progression through prostate cancer cell proliferation, survival and metastasis. It has been reported that high concentrations of circulating phosphorus are associated with an increased prostate cancer risk (21). As *SLC20A1* is a phosphorus transporter that brings phosphorus into cells, *SLC20A1* might play an important role in the uptake of phosphate required for prostate cancer cell proliferation.

PSA levels were not correlated with *SLC20A1* expression (Table III), which indicates that *SLC20A1* may play a role in malignancy that is independent of mechanisms regulating the PSA level. *SLC20A1* might serve as a biomarker for predicting prostate cancer which cannot be detected by PSA level. However, the specific role of *SLC20A1* in prostate cancer cells remain to be elucidated.

Notably, although our previous study showed that endocrine therapy is less effective for *SLC20A1*^{high} ER-positive breast cancer, no significant difference in DSS, DFS and PFS was identified between patients treated with endocrine therapy for *SLC20A1*^{high} and *SLC20A1*^{low} prostate cancer (Figure 2A and Table IV). The difference in sensitivity between prostate and breast cancer for patients with *SLC20A1*^{high} disease treated with endocrine therapy, albeit there are differences in androgen receptor-dependent and ER-dependent signaling pathways in these cancer types, should be resolved. On the other hand, as well as breast cancer subtypes such as basal-like, claudin-low, luminal A and luminal B (8, 12), in patients treated with radiotherapy, those with *SLC20A1*^{high} disease had a poorer prognosis than those with *SLC20A1*^{low} disease (Figure 2B and Table IV). ALDH1 is a detoxification enzyme degrading intracellular aldehyde, which is produced by reactive oxygen species (22, 23). High ALDH1 expression is correlated with a low level of reactive oxygen species in gastric cancer, lymphoma, breast cancer and melanoma cells (23-26). Cancer stem cells have stemness properties, including resistance to radiotherapy (27-30). *SLC20A1* has been shown to be involved in tumor-sphere formation by ALDH1-positive breast cancer stem cells (8). It is also known that ALDH1 is a cancer stem cell marker of prostate cancer (31). However, the specific role of *SLC20A1* in ALDH1 positive prostate cancer stem cells remains to be elucidated.

In conclusion, *SLC20A1* might serve as a prognostic biomarker for prostate cancer progression. Furthermore, the recommended treatment for patients with *SLC20A1*^{high} prostate cancer at the time of diagnosis appears to be endocrine therapy rather than radiotherapy, and *SLC20A1*^{high} status might be a biomarker suitable for decisions on selecting patients for endocrine therapy or radiotherapy.

Conflicts of Interest

The Authors have no conflicts of interest to declare.

Authors' Contributions

TO, CO, and IM performed the analyses; TO, CO, and KA conceived the study; C M AO, TK, YX, TS, YM, Ke. S, and ST performed validation; TO, CO, and KA drafted the article; TO, CO, IM, C M AO, TK, YX, YH, TS, YN, YM, SM, HI, Ke. S, ST, Ka. S, SO, and KA contributed to the discussion and review of the final article; all Authors approved the final article.

Acknowledgements

This work was supported by the Grant-in-Aid for Scientific Research (C) of Japan Society for the Promotion of Science (20K07207) (KA), JST Moonshot R&D (JPMJPS2022) (SO), Tokyo University of Science Grant for President's Research Promotion (KA), Grant-in-Aid for Research Activity Start-up (21K20732) (ST), JST SPRING (JPMJSP2151) (AO), Nagai Memorial Research Scholarship from the Pharmaceutical Society of Japan (AO) and a grant from the Consortium for Training Experts in Statistical Sciences (YN and SM).

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Received April 7, 2023

Revised May 13, 2023

Accepted May 23, 2023