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Prognostic and clinical significance of syndecan-1 expression in breast cancer: A systematic review and meta-analysis

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ABSTRACT

Background: The prognostic value of syndecan-1 (SDC1, also called CD138) in breast cancer remains controversial. Therefore, we performed a meta-analysis to assess the clinical significance of SDC1 expression in breast cancer.

Materials and methods: Various databases were searched to evaluate possible correlations between SDC1 protein or mRNA expression and prognostic significance in breast cancer. Pooled hazard ratios (HRs) and odds ratios (ORs) with 95% confidence intervals (CIs) were applied to perform a quantitative meta-analysis.

Results: A total of 1305 breast cancer patients from 9 eligible studies were included in this meta-analysis. Significant associations between elevated SDC1 protein expression and poor disease-free survival (DFS) (HR = 1.55, 95% CI: 1.12–2.14; P = 0.007) and overall survival (OS) (HR = 2.08, 95% CI: 1.61–2.69; P < 0.001) were observed. In addition, enhanced SDC1 protein expression correlated with negative estrogen receptor (ER) expression (OR, 2.38; 95% CI, 1.64–3.44; P < 0.001) and positive human epidermal growth factor receptor 2 (HER2) expression (OR, 1.77; 95% CI, 1.14–2.76; P = 0.01). However, increased SDC1 protein expression did not correlate with relapse-free survival (RFS) (HR = 0.33, 95% CI: 0.03–3.13; P = 0.33). There were no additional significant correlations observed between SDC1 protein expression and other clinical factors, including tumor size, lymph node involvement, nuclear grade, and progesterone receptor (PR) expression.

Conclusion: The results of this meta-analysis demonstrate that increased SDC1 protein expression in breast cancer is significantly associated with worse prognosis in terms of DFS and OS, and an aggressive phenotype is associated with negative ER expression and positive HER2 expression.

Introduction

Breast cancer remains a serious disease for females worldwide. It has been predicted that morbidity due to breast cancer in the United States in 2018 will account for 30% of all tumors affecting women [1]. Advances in our knowledge of breast cancer has led to the identification of several molecular markers for various breast cancer subtypes. These include estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67. As a result, treatment regimens and prognostic information have become more individualized according to breast cancer type [2]. In addition, molecular surrogates for breast cancer subtypes have successfully predicted prognostic significance in clinical practice [3]. However, breast cancer is a highly heterogeneous entity and the rates of satisfactory survival outcome remain to be improved. Thus, there is an urgent need for novel biomarkers to be identified and developed to provide additional treatment options for breast cancer.

Syndecan-1 (SDC1, also known as CD138) is a heparan sulfate proteoglycan (HSPG) that is one of four members of the syndecan family [4,5]. Previous studies have documented that SDC1 has

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pivotal roles in a variety of pathologic processes, including angiogenesis, cell proliferation, and cell migration [6,7]. Ibrahim et al. [8] targeted SDC1 with small interfering RNA in a triple-negative inflammatory breast cancer cell line, epidermal growth factor receptor (EGFR), Notch, and interleukin-6 (IL-6)/signal transducer and activator of transcription 3 (STAT3) signaling pathways were affected, providing insight into the role of SDC1 in breast cancer progression and dissemination. Numerous studies have also characterized the expression profile of SDC1 in various types of cancers, including breast cancer [9], hepatocellular carcinoma [10], colorectal cancer [11], lung cancer [12], ovarian cancer [13], prostate cancer [14], gallbladder cancer [15], and gastric cancer [16].

While it has been demonstrated that increased SDC1 expression is associated with an adverse prognosis in breast cancer [17,18], other studies have reported opposite results [19,20]. Therefore, in this study, the prognostic significance of SDC1 expression in breast cancer was investigated by performing a meta-analysis. The pooled results were subsequently verified with trial sequential and false-positive report probability (FPRP) analyses.

Materials and methods

Search strategy

Searches were conducted of the PubMed, Embase, Cochrane Library, and Web of Science databases through July 9, 2018. The search terms included, “breast neoplasms”/“breast cancer” and “syndecan-1“/“SDC1“/“CD138“.

Inclusion and exclusion criteria

Articles were selected according to the following criteria: (1) breast cancer patients were investigated, (2) the prognostic value of SDC1 expression was examined, and (3) studies provided sufficient prognostic information to extract hazard ratio (HR) and odds ratio (OR) with 95% confidence interval (CI). Reviews, duplicate studies, case reports, abstracts, or studies with insufficient data to investigate the relationship between prognostic factors and SDC1 expression in breast cancer were excluded.

Data extraction

Characteristics of eligible studies were extracted independently by two researchers. The main relevant information recorded included: author surname, year of publication, country where the study was conducted, number of patients, survival outcome, survival analysis method, cut-off values, and types of SDC1 antibody. Survival information was directly obtained from text and tables of the studies selected. When hazard ratios (HRs) were not directly reported, Engauge Digitizer Version 4.1 (http://markummitchell.github.io/engauge-digitizer/) software was used to extract them from Kaplan-Meier curves. To evaluate the quality of the included studies, Newcastle Ottawa Scale (NOS) criteria were applied [21]. Scores $\geq$7 indicate high quality.

Statistical analysis

Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were adopted in the present meta-analysis [22]. A method for extracting HRs from Kaplan-Meier curves suggested by Tierney et al. [23] was used. I^2 statistics and the Q-test were used to assess heterogeneity among eligible studies [24]. P-values < 0.05 and I^2 values > 50% were considered to indicate significant heterogeneity. A random effects model or fixed effects model was subsequently applied as appropriate [25]. Publication bias was evaluated with Begg's and Egger's tests [26,27]. Sensitivity was analyzed by removing one study at a time. Triple sequential analysis (TSA) and FPRP analysis were applied to verify true associations [28,29]. STATA version 12.0 (Stata Corporation, TX, USA) and Review Manager version 5.3 (Cochrane Collaboration, Copenhagen, Denmark) software programs were used to perform two-sided statistical tests. P-values less than 0.05 were considered to be statistically significant.

Results

Identification of relevant studies

A total of 565 potential studies were identified according to the search strategy described in the Methods. There were 196 duplicates studies which were excluded, as well as a total of 326 reviews, abstracts, and case reports. After reviewing the full text of the remaining 43 studies, 9 reviews, 12 studies with no endpoint, and 13 studies with insufficient data were additionally excluded. Therefore, a total of 9 studies involving 1305 patients were included in the present meta-analysis [17–20,30–34]. The selection process is presented in Fig. 1.

Characteristics of eligible studies

Primary characteristics of the included studies are summarized in Tables 1 and 2. All of the studies were observational in design and their cumulative NOS score was 7, indicating the studies were of high quality. All SDC1 mRNA expression studies were excluded for insufficient date. All nine eligible studies investigated the relationship between SDC1 protein expression and prognostic parameters of breast cancer. SDC1 protein expression was detected with immunohistochemistry (IHC), the antibodies and cut-off values used to detect SDC1 protein expression varied among the individual studies. Herein, the proportion of patients identified as having high SDC1 levels ranged from 19.7% to 83%.

Correlation between SDC1 protein expression and patient survival

Only two of the selected studies investigated a correlation between SDC1 protein expression and relapse-free survival (RFS) and no significant correlation was observed (HR = 0.33, 95% CI: 0.03–3.13; P = 0.33) (Fig. 2A). Due to significant heterogeneity of the data (P = 0.003, I^2 = 89%), a random-effects model was applied. Increased SDC1 protein expression was also found to be significantly associated with poor prognosis in terms of disease-free survival (DFS) (n = 3; HR = 1.55, 95% CI: 1.12–2.14; P = 0.007) (Fig. 2B) and overall survival (OS) (n = 5; HR = 2.08, 95% CI: 1.61–2.69; P < 0.001) (Fig. 2C) of breast cancer. Thus, a fixed effects model was applied because no obvious heterogeneity was observed (DFS, P = 0.25, I^2 = 29%; OS, P = 0.74, I^2 = 0%).

Correlation between SDC1 protein expression and other clinical factors

Correlations between elevated SDC1 protein expression and other clinical factors of breast cancer are comprehensively assessed (Table 3). In particular, up-regulation of SDC1 protein expression was found to be related to negative ER expression (n = 5; OR, 2.38; 95% CI, 1.64–3.44; P < 0.001). Conversely, enhanced SDC1 protein expression was found to correlate with positive HER2 expression (n = 4; OR, 1.77; 95% CI, 1.14–2.76; P = 0.01). For both correlations, a fixed effect model was applied due to an absence of significant heterogeneity (P = 0.40, I^2 = 1% and P = 0.16, I^2 = 43%, respectively).

There were no statistically significant correlations observed

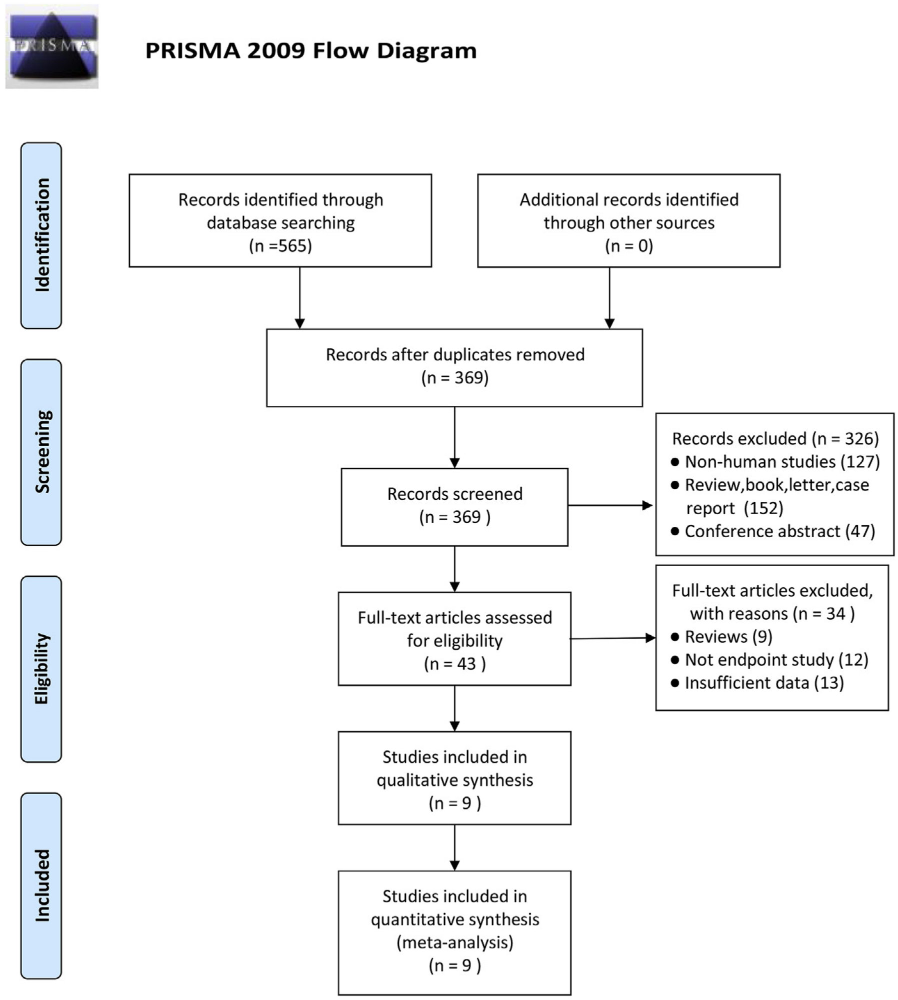

Fig. 1. Flow chart summarizing the study selection process used.

Table 1
Characteristics of eligible studies.

Publication	Year	Country	Cancer subtype	No. of patients	Median age, years (range)	Follow-up time, months (Median, range)	Outcome	Survival analysis	NOS (score)
Baba	2006	America	BC	207	58 (range, 23–87)	74.4	OS	K-M method	7
Barbareschi	2003	Italy	BC	254	56.1	86 (range, 6–178)	DFS, OS	Multivariate	8
Choi	2013	Korea	Invasive BC	100	49.5 (range, 29–77)	62.8 (range, 12.8–103.3)	DFS	Multivariate	7
Conklin	2018	America	DCIS	227	55.9	174 (range, 8.4–211.2)	RFS	K-M method	8
Leivonen	2014	Finland	Invasive BC	200	56.4 (range, 26–85)	208.8 (range, 33.6–240)	OS	K-M method	8
Lendorf	2011	Finland	BC	114	52 (range, 16–88)	NR	NR	NR	7
Lim	2014	Singapore	BC	61	52.2 (range, 28–90)	54	OS	K-M method	7
Loussouarn	2008	France	Invasive BC	80	72.7 (range, 44–95)	85.2 (range, 54–118.8)	RFS	Multivariate	8
Nguyen	2013	America	Advanced BC	62	52 (range, 30–83)	55.2	DFS, OS	K-M method	8

BC, breast cancer; DCIS, ductal carcinoma *in situ*; NR, not reported; RFS, relapse-free survival; DFS, disease-free survival; OS, overall survival; K-M, Kaplan-Meier; NOS, Newcastle Ottawa Scale.

between SDC1 protein expression and the other clinical parameters examined, including tumor size (n = 5, OR, 0.72; 95% CI, 0.42–1.24; P = 0.24), lymph node metastasis (n = 4, OR, 0.87; 95% CI, 0.43–1.78; P = 0.71), nuclear grade (n = 6, OR, 1.03; 95% CI, 0.47–2.22; P = 0.95), and PR expression (n = 5, OR, 0.88; 95% CI, 0.45–1.70; P = 0.70).

Publication bias and sensitivity analysis

No evidence of publication bias was detected according to Begg's test (DFS, P = 1.000; OS, P = 0.462) or Egger's test (DFS, P = 0.881; OS, P = 0.371). Moreover, the pooled HRs for both DFS (Fig. A.1A) and OS (Fig. A.1B) were verified in a sensitivity analysis.

Trial sequential and false-positive report probability (FPRP) analyses

A trial sequential analysis was performed to verify the pooled results of the meta-analysis. Both the cumulative *Z*-curve (blue line) crosses both the traditional boundary line and the trial sequential monitoring boundary (red line), and the cumulative information

Table 2
Methods of quantitative SDC1 measurement of eligible studies.

Publication	Year	SDC phenotype	Detection method	SDC1 expression	Staining location	Antibody	Cut-off value (low/high level)	High SDC1 expression
Baba	2006	SDC1	IHC	protein	Membrane and cytoplasmic location	anti-SDC1 (BB4,4 μg/ml, Serotec)	high (IHC score≥6.5)	26.2% (54/206)
Barbareschi	2003	SDC1	IHC	protein	Membrane,cytoplasmic,and both	anti-SDC1 (BB4, Serotec)	high (stained >10%)	42% (106/254)
Choi	2013	SDC1	IHC	protein	Membranous and cytoplasmic staining	anti-SDC1 (1:40, Abcam, UK)	high (stained >50%)	29% (29/100)
Conklin	2018	SDC1	IHC	protein	Stromal staining	anti-SDC1 (BB4, Serotec)	high (stained >21%)	55% (125/227)
Leivonen	2014	SDC1	IHC	protein	Stromal staining	anti-SDC1 (BB4, Serotec)	high (stained ≥5%)	39% (78/200)
Lendorf	2011	SDC1	IHC	protein	Stromal staining	anti-SDC1 (BB4, Abcam, UK)	high (stained ≥5%)	72.8% (83/114)
Lim	2014	SDC1	IHC	protein	Epithelial staining	anti-SDC1 (DL-101,Santa Cruz)	high (IRS >100)	19.7% (12/61)
Loussouarn	2008	SDC1	IHC	protein	Epithelial staining	anti-SDC1 (MI15,1:100,Dako)	high (stained >10%)	61.3% (49/80)
Nguyen	2013	SDC1	IHC	protein	Epithelial staining	anti-SDC1 (MI15,1:100,Dako)	high (stained ≥5%)	83% (51/62)

IHC, immunohistochemistry.

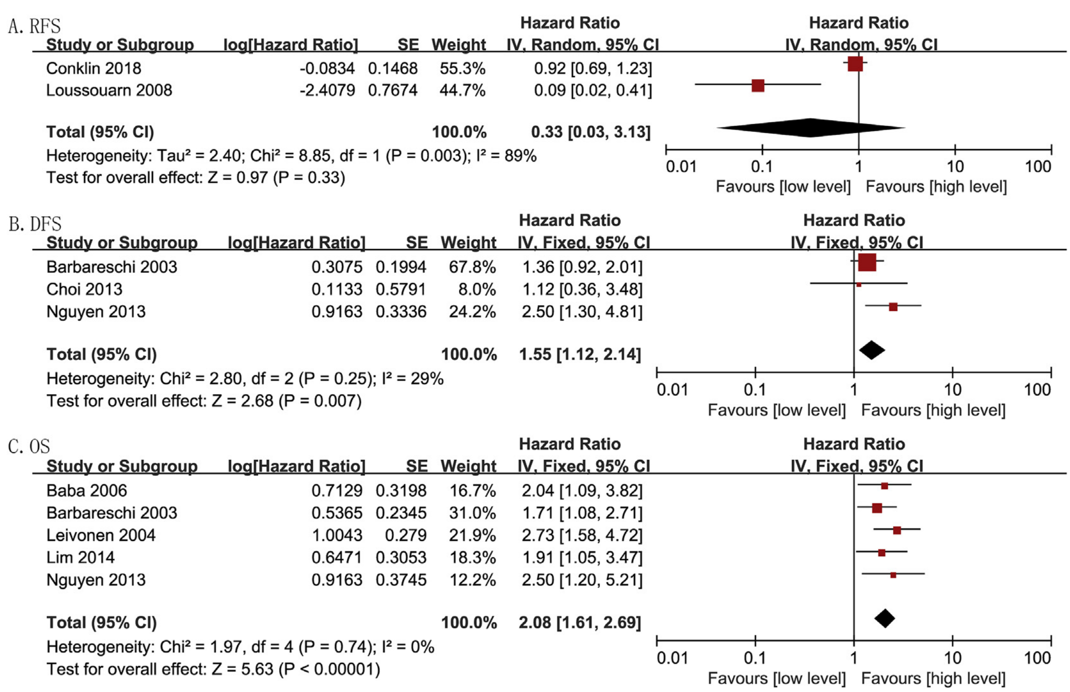

Fig. 2. Forest plots depicting correlations between SDC1 protein expression and (A) RFS, (B) DFS, and (C) OS among the breast cancer patients examined.

Table 3
Meta-analysis of the correlation between SDC1 expression and clinicopathological factors of breast cancer.

Clinicopathological parameter	No. of studies	No. of patients	OR (95% CI)	*P*-value	Heterogeneity	
					I^2 (%)	*P*-value
ER (- *vs.* +)	5	1108	2.38 (1.64–3.44)	<0.001	1	0.40
HER2 (+*vs.* -)	4	750	1.77 (1.14–2.76)	0.01	43	0.16
Tumor size (large *vs.* small)	5	831	0.72 (0.42–1.24)	0.24	0	0.59
Lymph node (+*vs.* -)	4	725	0.87 (0.43–1.78)	0.71	59	0.06
Nuclear grade (3 *vs.* 1 and 2)	6	1058	1.03 (0.47–2.22)	0.95	76	<0.001
PR (+*vs.* -)	5	1108	0.88 (0.45–1.70)	0.70	67	0.02

ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; OR, odds ratio.

reaches the required information size (RIS) for DFS (Fig. A.2A) and OS (Fig. A.2B).

In addition, survival outcomes were subjected to a FPRP analysis. With a prior probability of 0.01, only a positive association with OS was observed (FPRP < 0.001). Meanwhile, the FPRP values for RFS and DFS were both >0.2, indicating that these correlations were not truly significant (Table 4).

Table 4
False-positive report probability analysis for values of RFS, DFS, and OS.

Survival outcome	Crude HR (95% CI)	*P*-value	Statistical power	Prior probability				
				0.25	0.1	0.01	0.001	0.0001
RFS	0.33 (0.03–3.13)	0.334	0.270	0.788	0.918	0.992	0.999	1.000
DFS	1.55 (1.12–2.14)	0.007	0.421	0.052	0.142	0.645	0.948	0.995
OS	2.08 (1.61–2.69)	<0.001	0.006	<0.001	<0.001	<0.001	0.004	0.036

RFS, relapse-free survival; DFS, disease-free survival; OS, overall survival.

Discussion

To our knowledge, this is the first meta-analysis to examine a possible correlation between SDC1 protein expression and the prognosis and clinical parameters of breast cancer patients. Remarkably, in patients with increased SDC1 protein expression, their OS and DFS were found to correlate with worse prognosis. However, the results of the TSA and FPRP analyses that we performed only validated the OS correlation. Meanwhile, no meaningful correlation was identified between RFS and SDC1 protein expression. The latter result may be due to selection bias of the eligible studies involving RFS. For example, in one study [19], a correlation between RFS and SDC1 protein expression was found in early stage breast cancer patients with ductal carcinoma *in situ* (DCIS), while the mean age of included patients was 72.7 years in another study [20]. Therefore, the insignificant correlation between RFS and SDC1 protein expression might be owing to these selection bias. In addition, Tiemann et al. [35] reported that SDC1 protein expression did not correlate with RFS in DCIS of the breast, however, smoking was an important confounding factor influencing RFS ($P = 0.008$). Cui et al. [36] further demonstrated that higher levels of SDC1 mRNA expression were associated with a worse RFS, distant metastasis-free survival (DMFS), and OS in breast cancer based on an analysis of Kaplan-Meier data extracted from oncogene expression array datasets. Indeed, numerous studies have focused on the association between SDC1 expression and prognosis among various cancer patients. For example, in glioma patients, Shi et al. [37] observed a shorter survival period was associated with higher SDC1 protein expression. In prostate cancer, Szarvas et al. [38] also found that high levels of SDC1 protein expression were associated with adverse disease-specific survival (DSS) and OS. Hu et al. [39] demonstrated that SDC1 induces apoptosis by suppressing signaling via 3′-phosphoinositide-dependent kinase 1 (PDK1)/Akt/bad and docosahexaenoic acid in prostate cancer. However, Beauvais et al. [40] described the ability of SDC1 to inhibit apoptosis in myeloma cells via activation of the insulin like growth factor-1 receptor (IGF1R) signaling pathway. Similarly, enhanced stromal SDC1 protein expression was found to correlate with poor DSS and metastasis-free survival (MSS) in bladder cancer [41]. However, Parimon et al. [42] reported that high mRNA expression of SDC1 was associated with better OS in patients with lung cancer and Kim et al. [43] reported that strong SDC1 protein expression in the cytoplasm was related to better survival in cervical cancer. In addition, a meta-analysis conducted by Wei et al. [44], SDC1 protein expression was not found to correlate with prognosis in colorectal cancer patients. Thus, previous studies have demonstrated that the prognostic value of SDC1 expression varies among individual cancer types. This variability can be attributed to the various extents that SDC1 expression contributes to clinical pathological significance and signaling pathways in different tumors.

Additionally, we assessed possible correlations between elevated SDC1 protein expression and the clinicopathological parameters of the breast cancer patients examined. A notable observation was that enhanced SDC1 protein expression was associated with an aggressive breast cancer phenotype characterized by negative ER expression and positive HER2 expression. Malek-Hosseini et al. [45] also reported that SDC1 protein expression significantly correlates with breast tumor size. In addition, several studies [18,32] reported that higher levels of SDC1 protein expression positively correlated with a higher nuclear grade of breast cancer. This same aggressive phenotype was also found to encompass negative ER expression, positive HER2 expression, larger tumor size and higher nuclear grade in other studies [3,46–48], and to correlate with an adverse prognosis. Furthermore, this phenotype is consistent with the shorter DFS and OS that were observed for the breast cancer patients with these characteristics in the present study. Gotte et al. [49] further observed that the response of breast cancer patients with elevated SDC1 protein expression to neoadjuvant chemotherapy was reduced. However, numerous studies have demonstrated that pathological complete response rate can be an indicator of favorable prognosis in breast cancer [50,51]. Therefore, further investigations are needed to validate the efficacy of applying SDC1 inhibitors to enhance sensitivity to chemotherapy for breast cancer.

There were several limitations associated with this meta-analysis. First, the eligible studies were observational and published in English. These conditions may have led to recall bias and selection bias, respectively. Second, some of the HRs were extracted from Kaplan-Meier curves since they were not directly reported. This also may have impacted the stability of the pooled results. Finally, the involved sample size is relatively small in the meta-analysis.

In conclusion, the results of our meta-analysis indicate that an increase in SDC1 protein expression is associated with worse prognosis and an aggressive phenotype in breast cancer. Thus, the potential for SDC1 protein expression to serve as a prognostic indicator for breast cancer should be further investigated.

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Declarations of interest

None.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2018.12.019.

References

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics. Ca - Cancer J Clin 2018;68: 7–30. 2018.
[2] Coates AS, Winer EP, Goldhirsch A, et al. Tailoring therapies–improving the management of early breast cancer: St gallen international expert consensus on the primary therapy of early breast cancer 2015. Ann oncol 2015;26: 1533–46.
[3] Vasconcelos I, Hussainzada A, Berger S, et al. The St. Gallen surrogate classification for breast cancer subtypes successfully predicts tumor presenting features, nodal involvement, recurrence patterns and disease free survival. Breast 2016;29:181–5.
[4] Cordone I, Masi S, Summa V, et al. Overexpression of syndecan-1, MUC-1, and putative stem cell markers in breast cancer leptomeningeal metastasis: a cerebrospinal fluid flow cytometry study. Breast Cancer Res 2017;19:46.
[5] Szarvas T, Sevcenco S, Modos O, et al. Circulating syndecan-1 is associated with chemotherapy-resistance in castration-resistant prostate cancer. Urol Oncol 2018;36:312–9.
[6] Gharbaran R. Advances in the molecular functions of syndecan-1 (SDC1/ CD138) in the pathogenesis of malignancies. Crit Rev Oncol Hematol 2015;94: 1–17.
[7] Safadi RA, Quda BF, Hammad HM. Immunohistochemical expression of K6, K8, K16, K17, K19, maspin, syndecan-1 (CD138), alpha-SMA, and Ki-67 in ameloblastoma and ameloblastic carcinoma: diagnostic and prognostic correlations. Oral Surg Oral Med Oral Pathol Oral Radiol 2016;121:402–11.
[8] Ibrahim SA, Gadalla R, El-Ghonaimy EA, et al. Syndecan-1 is a novel molecular marker for triple negative inflammatory breast cancer and modulates the cancer stem cell phenotype via the IL-6/STAT3, Notch and EGFR signaling pathways. Mol cancer 2017;16:57.
[9] Schonfeld K, Herbener P, Zuber C, et al. Activity of indatuximab ravtansine against triple-negative breast cancer in preclinical tumor models. Pharm Res (N Y) 2018;35:118.
[10] Zeng Y, Liu X, Yan Z, et al. Sphingosine 1-phosphate regulates proliferation, cell cycle and apoptosis of hepatocellular carcinoma cells via syndecan-1. Prog Biophys Mol Biol 2017 Nov 24. https://doi.org/10.1016/j.pbiomolbio.2017.11.006. pii: S0079-6107(17)30218-3 [Epub ahead of print].
[11] Jary M, Lecomte T, Bouche O, et al. Prognostic value of baseline seric Syndecan-1 in initially unresectable metastatic colorectal cancer patients: a simple biological score. Int J Canc 2016;139:2325–35.
[12] Al-Shibli K, Al-Saad S, Andersen S, et al. The prognostic value of intraepithelial and stromal CD3-, CD117- and CD138-positive cells in non-small cell lung carcinoma. Apmis 2010;118:371–82.
[13] Kusumoto T, Kodama J, Seki N, et al. Clinical significance of syndecan-1 and versican expression in human epithelial ovarian cancer. Oncol rep 2010;23: 917–25.
[14] Brimo F, Vollmer RT, Friszt M, et al. Syndecan-1 expression in prostate cancer and its value as biomarker for disease progression. BJU Int 2010;106:418–23.
[15] Roh YH, Kim YH, Choi HJ, et al. Fascin overexpression correlates with positive thrombospondin-1 and syndecan-1 expressions and a more aggressive clinical course in patients with gallbladder cancer. J Hepatobiliary Pancreat Surg 2009;16:315–21.
[16] Chu YQ, Ye ZY, Tao HQ, et al. Relationship between cell adhesion molecules expression and the biological behavior of gastric carcinoma. World J Gastroenterol 2008;14:1990–6.
[17] Baba F, Swartz K, van Buren R, et al. Syndecan-1 and syndecan-4 are overexpressed in an estrogen receptor-negative, highly proliferative breast carcinoma subtype. Breast Canc Res Treat 2006;98:91–8.
[18] Barbareschi M, Maisonneuve P, Aldovini D, et al. High syndecan-1 expression in breast carcinoma is related to an aggressive phenotype and to poorer prognosis. Cancer-Am cancer soc 2003;98:474–83.
[19] Conklin MW, Gangnon RE, Sprague BL, et al. Collagen alignment as a predictor of recurrence after ductal carcinoma in situ. Cancer Epidemiol Biomark Prev 2018;27:138–45.
[20] Loussouarn D, Campion L, Sagan C, et al. Prognostic impact of syndecan-1 expression in invasive ductal breast carcinomas. Br J Canc 2008;98:1993–8.
[21] Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25:603–5.
[22] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg 2010;8:336–41.
[23] Tierney JF, Stewart LA, Ghersi D, et al. Practical methods for incorporating summary time-to-event data into meta-analysis. Trials 2007;8:16.
[24] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
[25] DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. Contemp Clin Trials 2015;45:139–45.
[26] Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088–101.
[27] Egger M, Davey SG, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
[28] Wetterslev J, Thorlund K, Brok J, et al. Trial sequential analysis may establish when firm evidence is reached in cumulative meta-analysis. J Clin epidemiol 2008;61:64–75.
[29] Wacholder S, Chanock S, Garcia-Closas M, et al. Assessing the probability that a positive report is false: an approach for molecular epidemiology studies. J Natl Cancer Inst 2004;96:434–42.
[30] Choi EJ, Yun JA, Jeon EK, et al. Prognostic significance of RSPO1, WNT1, P16, WT1, and SDC1 expressions in invasive ductal carcinoma of the breast. World J Surg oncol 2013;11:314.
[31] Leivonen M, Lundin J, Nordling S, et al. Prognostic value of syndecan-1 expression in breast cancer. Oncology-basel 2004;67:11–8.
[32] Lendorf ME, Manon-Jensen T, Kronqvist P, et al. Syndecan-1 and syndecan-4 are independent indicators in breast carcinoma. J Histochem cytochem 2011;59:615–29.
[33] Lim GH, Tan PH, Jara-Lazaro AR, et al. Syndecan-1 is a potential biomarker for triple-positive breast carcinomas in Asian women with correlation to survival. Singapore Med J 2014;55:468–72.
[34] Nguyen TL, Grizzle WE, Zhang K, et al. Syndecan-1 overexpression is associated with nonluminal subtypes and poor prognosis in advanced breast cancer. Am J Clin pathol 2013;140:468–74.
[35] Tiemann K, Weigel MT, Alkatout I, et al. Significance of syndecan-1 expression in ductal carcinoma in situ of the breast. Anticancer Res 2014;34:3607–16.
[36] Cui X, Jing X, Yi Q, et al. Clinicopathological and prognostic significance of SDC1 overexpression in breast cancer. Oncotarget 2017;8:111444–55.
[37] Shi S, Zhong D, Xiao Y, et al. Syndecan-1 knockdown inhibits glioma cell proliferation and invasion by deregulating a c-src/FAK-associated signaling pathway. Oncotarget 2017;8:40922–34.
[38] Szarvas T, Reis H, Vom DF, et al. Soluble syndecan-1 (SDC1) serum level as an independent pre-operative predictor of cancer-specific survival in prostate cancer. Prostate 2016;76:977–85.
[39] Hu Y, Sun H, Owens RT, et al. Syndecan-1-dependent suppression of PDK1/ Akt/bad signaling by docosahexaenoic acid induces apoptosis in prostate cancer. Neoplasia 2010;12:826–36.
[40] Beauvais DM, Jung O, Yang Y, et al. Syndecan-1 (CD138) Suppresses apoptosis in multiple myeloma by activating IGF1 receptor: prevention by SynstatinIGF1R inhibits tumor growth. Cancer Res 2016;76:4981–93.
[41] Szarvas T, Reis H, Kramer G, et al. Enhanced stromal syndecan-1 expression is an independent risk factor for poor survival in bladder cancer. Hum pathol 2014;45:674–82.
[42] Parimon T, Brauer R, Schlesinger SY, et al. Syndecan-1 controls lung tumorigenesis by regulating miRNAs packaged in exosomes. Am J Pathol 2018;188: 1094–103.
[43] Kim YI, Lee A, Lee BH, et al. Prognostic significance of syndecan-1 expression in cervical cancers. J. Gynecol Oncol 2011;22:161–7.
[44] Wei HT, Guo EN, Dong BG, et al. Prognostic and clinical significance of syndecan-1 in colorectal cancer: a meta-analysis. BMC Gastroenterol 2015;15: 152.
[45] Malek-Hosseini Z, Jelodar S, Talei A, et al. Elevated Syndecan-1 levels in the sera of patients with breast cancer correlate with tumor size. Breast Cancer-tokyo 2017;24:742–7.
[46] Ehinger A, Malmstrom P, Bendahl PO, et al. Histological grade provides significant prognostic information in addition to breast cancer subtypes defined according to St Gallen 2013. Acta Oncol 2017;56:68–74.
[47] Viot J, Bachour M, Meurisse A, et al. Follow-up of patients with localized breast cancer and first indicators of advanced breast cancer recurrence: a retrospective study. Breast 2017;34:53–7.
[48] Ono M, Tsuda H, Yoshida M, et al. Prognostic significance of progesterone receptor expression in estrogen-receptor positive, HER2-negative, node-negative invasive breast cancer with a low ki-67 labeling index. Clin Breast cancer 2017;17:41–7.
[49] Gotte M, Kersting C, Ruggiero M, et al. Predictive value of syndecan-1 expression for the response to neoadjuvant chemotherapy of primary breast cancer. Anticancer Res 2006;26:621–7.
[50] Tian M, Zhong Y, Zhou F, et al. Effect of neoadjuvant chemotherapy in patients with triple-negative breast cancer: a meta-analysis. Oncol lett 2015;9: 2825–32.
[51] Broglio KR, Quintana M, Foster M, et al. Association of pathologic complete response to neoadjuvant therapy in HER2-positive breast cancer with long-term outcomes: a meta-analysis. Jama oncol 2016;2:751–60.