Systematic Review and Meta-Analysis

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NY-ESO-1 expression in solid tumors predicts prognosis

A systematic review and meta-analysis

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Abstract

Background: New York esophageal squamous cell carcinoma 1 (NY-ESO-1) is a member of the cancer testis antigen family. NY-ESO-1 has documented potential as an effective target for cancer immunotherapy. The prognostic value of NY-ESO-1 expression in solid tumors, however, remains controversial because of inconclusive data.

Methods: For this analysis, the Medline, Embase, and Cochrane Library databases were searched up to February 2018 for studies investigating NY-ESO-1 expression in solid tumors and overall survival (OS), progression-free survival (PFS), or disease-free survival (DFS). Hazard ratios (HRs) with 95% confidence intervals (CIs) were extracted from each study. Pooled HRs and CIs were calculated using the Mantel-Haenszel fixed effects or random effects model.

Results: A total of 23 studies were included in the analysis. The combined HR (95% CI) estimates for OS, PFS, and DFS were 1.41 (95% CI: 1.24–1.61; $I^2=0\%$), 1.62 (95% CI: 1.42–1.84; $I^2=17\%$), and 0.95 (95% CI: 0.56–1.59; $I^2=57\%$), respectively.

Conclusions: NY-ESO-1 expression in solid tumors is associated with worse OS and PFS. Studies are still needed to provide more evidence.

Abbreviations: CI = confidence interval, CSC = cancer stem cell, CTA = cancer testis antigen, DFS = disease-free survival, HR = hazard ratio, MSC = mesenchymal stem cell, NY-ESO-1 = New York esophageal squamous cell carcinoma 1, OS = overall survival, PFS = progression-free survival, SE = standard error.

Keywords: meta-analysis, New York esophageal squamous cell carcinoma 1, solid tumor, survival

1. Introduction

New York esophageal squamous cell carcinoma 1 (NY-ESO-1) is a protein consisting of 180 amino acids, and its gene is located in the Xq28 region of the X chromosome. As a member of the cancer testis antigen (CTA) family, NY-ESO-1 has been shown to be expressed in spermatogonia, primary spermatocytes, oogonia, and placenta and in a variety of cancers, such as melanoma, ovarian cancer, cervical cancer, etc.[1,2] The blood-testis barrier makes the testis an immune privileged organ. In view of this property, NY-ESO-1 is believed to be a promising target for cancer immunotherapy, and it has been widely researched since its discovery. Accumulating evidence indicates that NY-ESO-1 is one of the most immunogenic antigens in the tumor-associated antigen family.[3] Therefore, multiple clinical trials with variable results have been carried out to advance the bedside application of NY-ESO-1-based cancer immunotherapy.[4–6]

Unlike the unambiguous immunogenicity of NY-ESO-1, the prognostic relevance of its expression in solid tumors, however, remains controversial. Varied survival outcomes have been reported in studies focused on the prognostic value of NY-ESO-1 expression. Therefore, we conducted the first comprehensive meta-analysis of published literature on this topic to summarize the evidence.

2. Materials and methods

The study was approved by the Committees for the Ethical Review of Research at the Wuxi People's Hospital.

2.1. Literature search

The Medline, Embase, and Cochrane libraries were searched in October 2018. The following keywords were combined: "NY-ESO-1," "New York Esophageal Squamous Cell Carcinoma 1," and "survival." No language or time restrictions were implemented.

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HW, DC, and RW contributed equally to this study.

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2.2. Inclusion criteria

In order to be eligible, studies had to discuss the relevance of NY-ESO-1 expression to survival and provide sufficient data for extracting or estimating the hazard ratio (HR) and 95% confidence interval (CI).

2.3. Exclusion criteria

Studies were excluded from the analysis if the articles were not written in English, the articles were reviews or letters, the studies did not investigate solid tumors, or primary data could not be extracted or used to calculate essential information for the meta-analysis.

2.4. Data extraction

The primary data were the HR and 95% CI of survival outcomes [overall survival (OS), progression-free survival (PFS), and disease-free survival (DFS)]. OS: the length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive. PFS: the length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. DFS: the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer. Three reviewers (HW, DC, and Wen Quan) independently extracted the primary data and baseline characteristics from the included studies. Only Kaplan-Meier survival curves, not the HR and 95% CI, were provided in some included articles. For these articles, methods based on the work of Parmar et al,[7] Williamson et al,[8] and Tierney et al[9] were used to calculate the HR. The baseline characteristics included the first author, publication year, tumor type, study size, methods to detect NY-ESO-1 expression, percentage of patients with positive NY-ESO-1 expression, and HR estimation methods. Disagreements were resolved by discussion.

2.5. Statistical methods

The logHR and standard error were calculated using software designed by Matthew Sydes and Jayne Tierney (Medical Research Council Clinical Trials Unit, London, UK).[9] The pooled HR was obtained using fixed or random effects models depending on the presence of heterogeneity among studies. Heterogeneity was evaluated with Cochran Q test and the I^2 index and was defined as $P < .10$ or $I^2 > 50\%$.[10]

Forrest plots showed the pooled HR. HR > 1 indicated worse survival outcomes. Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of the included studies. Funnel plot, Begg test, and Egger test were conducted to predict the publication bias. All calculations were conducted using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK) and Stata Software 11.0 (Stata, College Station, TX).

As a validation, we also used www.kmplot.com Web site to explore the relationship between the expression of NY-ESO-1 mRNA and prognosis. Data of this Web site were based on TCGA database.

3. Results

3.1. Characteristics of eligible studies

A total of 134 articles were obtained from the literature search. After the title and abstract were read and the full text was reviewed, 23 studies were included (Fig. 1).[11–33] Eligible studies investigated synovial sarcoma, melanoma, adenoid cystic carcinoma of the head and neck, ovarian cancer, breast cancer, non–small cell lung cancer (NSCLC), head and neck squamous

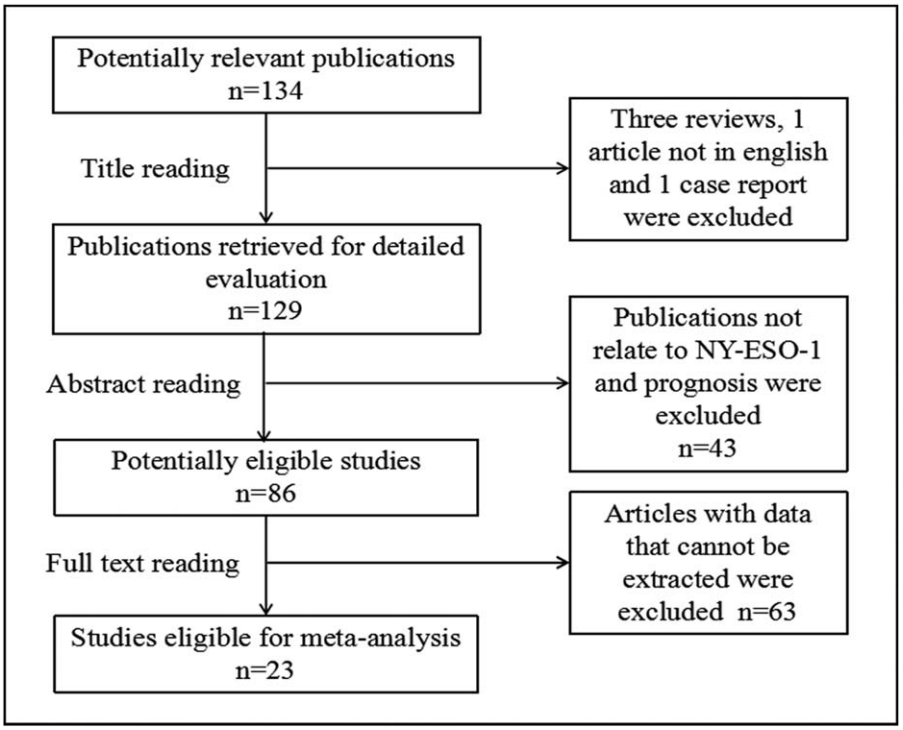

Figure 1. Flowchart of study selection.

Table 1

Studies involved in the meta-analysis.

Study	Year	Country	Tumors	Study size (positive rate)	Detection method	Epitope	Survival data	HR estimation	Cut-off value	NOS score
Szender et al[11]	2017	USA	Ovarian cancer	1002 (40.7%)	RT-PCR/IHC	ES121	OS/PFS	Extrapolated/ reported	Positive: a minimum of 5% cells positive	8
Mori et al[12]	2017	Japan	Melanoma	22 (63.6%)	IHC	E978	OS	Extrapolated	Positive: a minimum of 5% cells positive	6
Veit et al[13]	2016	Germany	Adenoid cystic carcinoma of the head and neck	84 (57.1%)	IHC	E978	OS/PFS	Extrapolated	Positive: the intensity was 1+ in >10% cells	6
Lee et al[14]	2015	Korea	Triple-negative breast cancer	609 (9.7%)	IHC	E978	OS/DFS	Reported	Positive: immunoreactive scores not less than 1	7
Grah et al[15]	2014	Croatia	NSCLC	80 (18.8%)	IHC	B9.8	OS	Extrapolated	Positive: not less than 11% of tumor cells were positive	6
Laban et al[16]	2014	Germany	Head and neck squamous cell carcinoma	305 (4.3%)	IHC	E978	OS	Extrapolated	Positive: the intensity was 1+ in >10% cells	8
Gjerstorff et al[17]	2013	Denmark	NSCLC	169 (11.8%)	IHC	E978	OS	Extrapolated	Positive: if staining was observed	8
John et al[18]	2013	Australia	NSCLC	106 (24.8%)	IHC	E978	OS	Reported	Positive: if staining was observed	7
Liang et al[19]	2013	China	Hepatocellular carcinoma	362 (14.6%)	IHC	E978	OS	Extrapolated	Positive: if staining was observed	8
Balafoutas et al[20]	2013	Germany	Breast cancer	140 (15.0%)	IHC	E978	OS/DFS	Reported	Positive: a minimum of 5% cells positive	8
Ademuyiwa et al[21]	2012	USA	Triple-negative breast cancer	168 (16.1%)	IHC	/	OS/PFS	Extrapolated	Positive: if staining was observed	6
Dyrskjøt et al[22]	2012	Denmark	Urothelial carcinoma	346 (34.4%)	RT-PCR	/	PFS	Reported	Positive: the expression level of the 1%	8
Zhou et al[23]	2011	China	Intrahepatic cholangiocarcinoma	89 (21.3%)	IHC	E978	OS	Extrapolated	Positive: a minimum of 5% cells positive	7
Pastorcic-Grgic et al[24]	2009	Croatia	Pharyngeal cancer	90 (33.3%)	IHC	B9.8.1.1	DFS	Extrapolated	Positive: if staining was observed	6
Kim et al[25]	2009	Korea	NSCLC	129 (17.8%)	IHC	E978	OS	Extrapolated	Not mentioned	6
Napoletano et al[26]	2008	Italy	Cervical cancer	109 (46.8)	IHC	D8.38	OS	Extrapolated	Positive: a minimum of 5% cells positive	7
Bellati et al[27]	2007	Italy	Vulvar cancer	59 (67.8%)	IHC	D8.38	OS/PFS	Extrapolated	Positive: a minimum of 5% cells positive	7
Velazquez et al[28]	2007	USA	Melanoma	56 (32.1%)	IHC	E978	OS	Extrapolated	Positive: if staining was observed	6
Yakirevich et al[29]	2003	Israel	Serous ovarian neoplasms	53 (18.9%)	IHC	D8.38	OS	Extrapolated	Positive: a minimum of 5% cells positive	8
Gure et al[30]	2005	USA	NSCLC	220 (10.0%)	RT-PCR	/	OS	Reported	Positive: at least 1 fg of transcript per 2 μg of mRNA	6
Akcakanat et al[31]	2006	Japan	Esophageal cancer	213 (20.7%)	IHC	E978	OS	Extrapolated	Positive: a minimum of 5% cells positive	8
Fujita et al[32]	2004	Japan	Esophageal cancer	64 (40.6%)	IHC	ES121	OS	Extrapolated	Positive: a minimum of 5% cells positive	8
Iura et al[33]	2017	Japan	Synovial sarcoma	99 (62.6%)	IHC	E978	OS/DFS	Extrapolated	Positive: a total score of 3 or higher	7

DFS = disease-free survival, HR = hazard ratio, NOS = Newcastle-Ottawa Scale, NSCLC = non–small cell lung cancer, OS = overall survival, PFS = progression-free survival.

cell carcinoma, hepatocellular carcinoma, urothelial carcinoma, intrahepatic cholangiocarcinoma, pharyngeal cancer, cervical cancer, vulvar cancer, and esophageal cancer. The sample size ranged from 22 to 1002 patients. The included studies were conducted between 2003 and 2017. All of the included studies were retrospective. The main features of these studies including cut-off value and NOS score of each study are listed in Table 1.

3.2. NY-ESO-1 expression and overall survival

Twenty-one of the 23 included studies evaluated the association of NY-ESO-1 expression with OS.[11–21,23,25–33] The HR and 95% CI were provided in 4 studies enrolling patients with breast cancer or NSCLC.[14,18,20,30] In the other studies, the HR and 95% CI were extracted from the given Kaplan-Meier survival curve. A fixed effects model was used, and the pooled HR (positive vs negative) was 1.41 (95% CI: 1.24–1.61; I^2 = 0%, P = .54; Fig. 2A). The results showed increased mortality among solid tumor patients with positive NY-ESO-1 expression. The funnel plot showed no obvious publication bias (Fig. 3A). The Begg test (P = .778) and Egger test (P = .589) also revealed no significant publication bias.

3.3. NY-ESO-1 expression and progression-free survival

Five of the included studies investigated PFS.[11,13,21–22,27] Four of these studies directly reported the HR and 95% CI.[11,14,20,22] Survival data for the other studies were acquired using the method developed by Matthew Sydes and Jayne Tierney. HRs (positive vs negative) of PFS were pooled by a fixed effects model (Fig. 2B). The results (pooled HR: 1.62; 95% CI: 1.42–1.84; I^2 = 17%, P = .31) demonstrated that positive NY-ESO-1 expression in tumor tissue indicated worse PFS. No obvious publication bias was found in the funnel plot (Fig. 3B). The Begg test (P = .806) and Egger test (P = .515) showed no significant publication bias.

3.4. NY-ESO-1 expression and disease-free survival

Four of the included studies investigated PFS.[14,20,24,33] In contrast to the OS and PFS results, the pooled HR for DFS was 0.95 (95% CI: 0.56–1.59; I^2 = 57%, P = .07), which indicated a nonstatistically significant trend of the beneficial effect of NY-ESO-1 expression (Fig. 2C). The funnel plot (Fig. 3C), Begg test (P = .308) and Egger test (P = .211) found no significant publication bias.

3.5. NY-ESO-1 mRNA level and OS

We searched the Web site www.kmplot.com and the analysis based on TCGA database in this Web revealed that high level NY-ESO-1 mNRA predicted poor prognosis in lung adenocarcinoma patients [HR 2.67, 95% CI (1.31–5.44), P = .005].

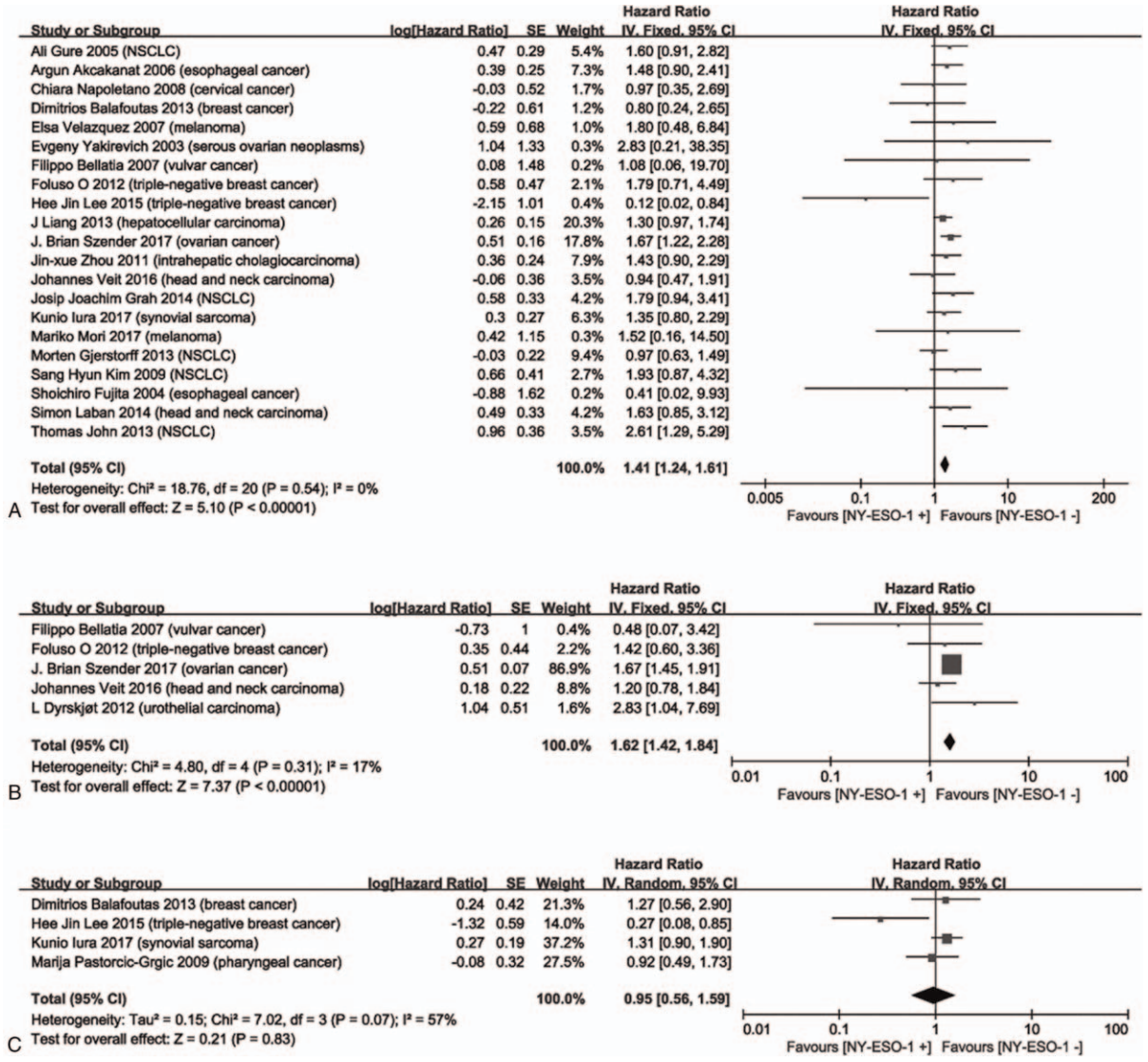

Figure 2. Forrest plots of estimated hazard ratios (HRs) for (A) New York esophageal squamous cell carcinoma 1 (NY-ESO-1) expression and overall survival (OS), (B) NY-ESO-1 expression and progression-free survival (PFS), and (C) NY-ESO-1 expression and disease-free survival (DFS). CI = confidence interval, NSCLC = non–small cell lung cancer.

4. Discussion

As far as we know, this is the first meta-analysis discussed the prognostic value of NY-ESO-1 expression. Heterogeneity exists in NY-ESO-1 expression among different histological types of tumors. The highest NY-ESO-1 expression rate was previously reported as up to 82% in neuroblastoma.[34] In the present article, the included studies used either immunohistochemistry or Quantitative Real-time PCR to detect NY-ESO-1 expression, and the expression rate ranged from 4.3% (head and neck squamous cell carcinoma)[16] to 67.8% (vulvar cancer).[27] Five included studies on the same cancer type (NSCLC) showed different expression rates, ranging from 10.0% to 24.8%, among patients,[15,17–18,25,30] similar to the varied result which is reported by another study.[2] As a subgroup, we analyzed the OS predictive value of NY-ESO-1 expression in NSCLC patients. The pooled HR (positive vs negative) was 1.48 (95% CI: 1.14–1.92; $I^2 = 43\%$, $P = .14$), which also revealed a worse outcome in NY-ESO-1-positive NSCLC patients. Consistently, the analysis of kmplot.com Web site data also suggests that high level NY-ESO-1 mRNA is associated with poor prognosis. Heterogeneity in NY-ESO-1 expression in a certain tumor type may be due to detection methodology. Immunohistochemical methods have adopted different antibodies against certain epitopes of NY-ESO-1, such as E978, ES121, B.9.8.1.1, and D8.38. In addition, Laban et al[16] discussed NY-ESO-1 protein localization in their study. The survival outcomes of the cytoplasmic and nuclear co-expression group and the cytoplasmic or nuclear-only expression groups were compared to those of the negative expression group, and a statistically significant shorter OS was discovered in the co-expression group. The present study, however, pooled the HRs of only the single location (nuclear or cytoplasmic) expression group to minimize heterogeneity among the included articles. Cochran Q test ($P = .54/.31$) and the I^2 index ($I^2 = 0\%/17\%$) for the pooled analysis of OS/PFS showed that the heterogeneity among the included studies was acceptable. For the pooled analysis of DFS, the Q test ($P = .07$) and I^2 index ($I^2 = 57\%$)

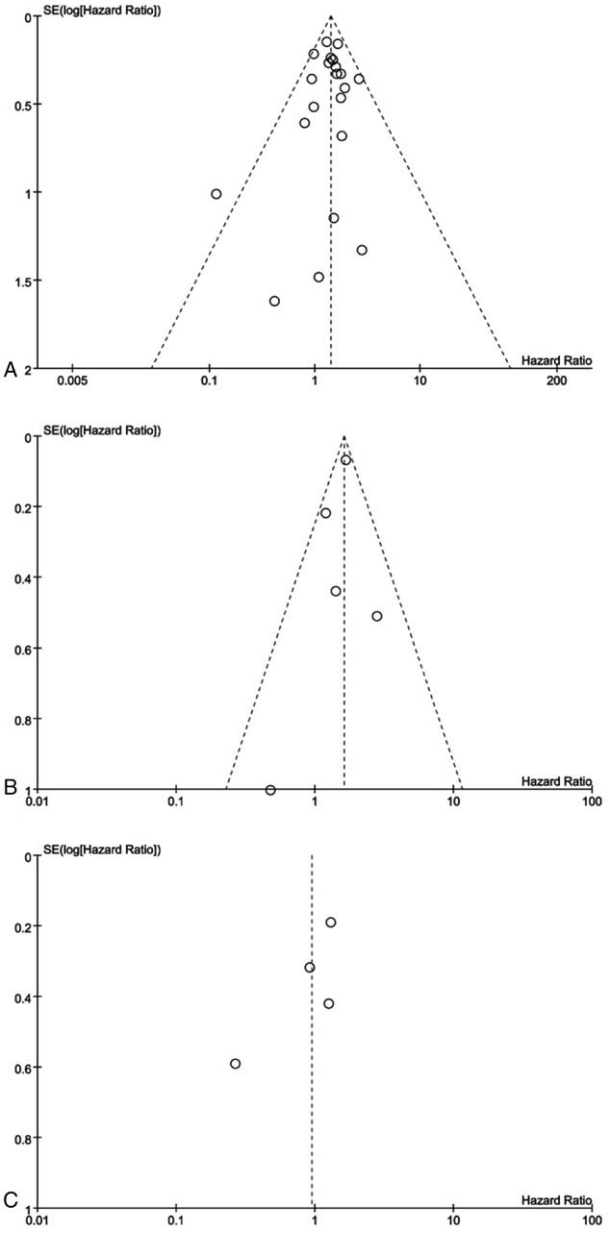

Figure 3. Funnel plots for studies of (A) New York esophageal squamous cell carcinoma 1 (NY-ESO-1) expression and overall survival (OS), (B) NY-ESO-1 expression and progression-free survival (PFS), and (C) NY-ESO-1 expression and disease-free survival (DFS).

tended to indicate that random effects models should be used to calculate the pooled HR.

The correlation of NY-ESO-1 expression and survival may be caused by the biological function of NY-ESO-1 in cancer cells, which has not been fully elucidated. According to the specific expression in spermatogonia and primary spermatocytes and the lack of expression in differentiated spermatids in the testis, it is speculated that NY-ESO-1 may play a role in germ cell self-renewal or differentiation.[35] In terms of cancer cells, a specific interaction has been discovered between NY-ESO-1 and another CTA, melanoma antigen gene C1 (*MAGE-C1*), which is believed to play a role in cell cycle progression and apoptosis.[36,37] In addition, NY-ESO-1 expression in mesenchymal stem cells (MSCs) has been documented by immunofluorescence analysis of bone marrow cells.[38] Cancer stem cells (CSCs) are similar to MSCs and possess self-renewal ability and differentiation potential, which are closely related to therapeutic resistance in cancer. Through a study on CSCs isolated from glioma cell lines and tissues, Yawata et al[39] found stronger and more frequent expression of NY-ESO-1 in CSCs than in differentiated cells. This evidence may partially explain the increased mortality and worse PFS of patients with NY-ESO-1-positive solid tumors. The opposite result for DFS may be attributed to the relatively small sample size enrolled. Therefore, the biological function of NY-ESO-1 in cancer cells and the prognostic value of NY-ESO-1 expression still need to be further investigated.

Limitations of the present meta-analysis need to be discussed. First, the HR and 95% CI of some included studies were extracted, and log(HR) and se(log(HR)) were then calculated by software provided by Matthew Sydes and Jayne Tierney. Potential biases may relate to this process. Second, only 23 studies met the inclusion criteria, and these studies investigated 13 different types of cancer. In the future, more studies could be added to our meta-analysis to validate the present results, and subgroup analysis should be conducted according to tumor type. Finally, our meta-analysis used only published data. Updated individual patient data were not obtained; if those data were added to our analysis, the accuracy and validity could be improved.

In conclusion, our meta-analysis suggests that NY-ESO-1 expression in solid tumors has prognostic value. Positive NY-ESO-1 expression could predict shorter OS and PFS. No significant prediction ability for DFS was found. More high-quality studies are eagerly needed to elucidate the biological function of NY-ESO-1 and to provide more evidence of its prognostic value.

Author contributions

Data curation: Huiyu Wang, Datian Chen, Dandan Xia.
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Writing – review and editing: Huiyu Wang, Runjie Wang, Chaoying Liu.

References

[1] Wang HY, Wang RF. Immune targets and neoantigens for cancer immunotherapy and precision medicine. Cell Res 2016;27:11–37.
[2] Esfandiary A, Ghafouri-Fard S. New York esophageal squamous cell carcinoma-1 and cancer immunotherapy. Immunotherapy 2015;7: 411–39.
[3] Grizzi F, Mirandola L, Qehajaj D, et al. Cancer-testis antigens and immunotherapy in the light of cancer complexity. Int Rev Immunol 2015;34:143–53.
[4] Davis ID, Chen W, Jackson H, et al. Recombinant NY-ESO-1 protein with ISCOMATRIX adjuvant induces broad integrated antibody and CD4(+) and CD8(+) T cell responses in humans. Proc Natl Acad Sci USA 2004;101:10697–702.

[5] Nicholaou T, Ebert LM, Davis ID, et al. Regulatory T-cell mediated attenuation of T-cell responses to the NY-ESO-1 ISCOMATRIX vaccine in patients with advanced malignant melanoma. Clin Cancer Res 2009;15:2166–73.
[6] Aoki M, Ueda S, Nishikawa H, et al. Antibody responses against NY-ESO-1 and HER2 antigens in patients vaccinated with combinations of cholesteryl pullulan (CHP)- NY-ESO-1 and CHP-HER2 with OK-432. Vaccine 2009;27:6854–61.
[7] Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. Stat Med 1998;17:2815–34.
[8] Williamson PR, Smith CT, Hutton JL, et al. Aggregate data meta-analysis with time-to-event outcomes. Stat Med 2002;21:3337–51.
[9] Tierney JF, Stewart LA, Ghersi D, et al. Practical methods for incorporating summary time-to-event data into meta-analysis. Trials 2007;8:16.
[10] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
[11] Szender JB, Papanicolau-Sengos A, Eng KH, et al. NY-ESO-1 expression predicts an aggressive phenotype of ovarian cancer. Gynecol Oncol 2017;145:420–5.
[12] Mori M, Funakoshi T, Kameyama K, et al. Lack of XAGE-1b and NY-ESO-1 in metastatic lymph nodes may predict the potential survival of stage III melanoma patients. J Dermatol 2017;44:671–80.
[13] Veit J, Heine D, Thierauf J, et al. Expression and clinical significance of MAGE and NY-ESO-1 cancer-testis antigens in adenoid cystic carcinoma of the head and neck. Head Neck 2016;38:1008–16.
[14] Lee HJ, Kim JY, Song IH, et al. Expression of NY-ESO-1 in triple-negative breast cancer is associated with tumor-infiltrating lymphocytes and a good prognosis. Oncology 2015;89:337–44.
[15] Grah JJ, Katalinic D, Juretic A, et al. Clinical significance of immunohistochemical expression of cancer/testis tumor-associated antigens (MAGE-A1, MAGE-A3/4, NY-ESO-1) in patients with non-small cell lung cancer. Tumori 2014;100:60–8.
[16] Laban S, Atanackovic D, Luetkens T, et al. Simultaneous cytoplasmic and nuclear protein expression of melanoma antigen-A family and NY-ESO-1 cancer-testis antigens represents an independent marker for poor survival in head and neck cancer. Int J Cancer 2014;135:1142–52.
[17] Gjerstorff MF, Pøhl M, Olsen KE, et al. Analysis of GAGE, NY-ESO-1 and SP17 cancer/testis antigen expression in early stage non-small cell lung carcinoma. BMC Cancer 2013;13:466.
[18] John T, Starmans MH, Chen YT, et al. The role of cancer-testis antigens as predictive and prognostic markers in non-small cell lung cancer. PLoS One 2013;8:e67876.
[19] Liang J, Ding T, Guo ZW, et al. Expression pattern of tumour-associated antigens in hepatocellular carcinoma: association with immune infiltration and disease progression. Br J Cancer 2013;109:1031–9.
[20] Balafoutas D, Zur Hausen A, Mayer S, et al. Cancer testis antigens and NY-BR-1 expression in primary breast cancer: prognostic and therapeutic implications. BMC Cancer 2013;13:271.
[21] Ademuyiwa FO, Bshara W, Attwood K, et al. NY-ESO-1 cancer testis antigen demonstrates high immunogenicity in triple negative breast cancer. PLoS One 2012;7:e38783.
[22] Dyrskjøt L, Zieger K, Lildal TK, et al. Expression of MAGE-A3, NY-ESO-1, LAGE-1 and PRAME in urothelial carcinoma. Br J Cancer 2012;107:116–22.
[23] Zhou JX, Li Y, Chen SX, et al. Expression and prognostic significance of cancer-testis antigens (CTA) in intrahepatic cholagiocarcinoma. J Exp Clin Cancer Res 2011;30:2.
[24] Pastorcic-Grgic M, Sarcevic B, Dosen D, et al. Prognostic value of MAGE-A and NY-ESO-1 expression in pharyngeal cancer. Head Neck 2010;32:1178–84.
[25] Kim SH, Lee S, Lee CH, et al. Expression of cancer-testis antigens MAGE-A3/6 and NY-ESO-1 in non-small-cell lung carcinomas and their relationship with immune cell infiltration. Lung 2009;187:401–11.
[26] Napoletano C, Bellati F, Tarquini E, et al. MAGE-A and NY-ESO-1 expression in cervical cancer: prognostic factors and effects of chemotherapy. Am J Obstet Gynecol 2008;198: 99.e1-7.
[27] Bellati F, Napoletano C, Tarquini E, et al. Cancer testis antigen expression in primary and recurrent vulvar cancer: association with prognostic factors. Eur J Cancer 2007;43:2621–7.
[28] Velazquez EF, Jungbluth AA, Yancovitz M, et al. Expression of the cancer/testis antigen NY-ESO-1 in primary and metastatic malignant melanoma (MM)—correlation with prognostic factors. Cancer Immun 2007;7:11.
[29] Yakirevich E, Sabo E, Lavie O, et al. Expression of the MAGE-A4 and NY-ESO-1 cancer-testis antigens in serous ovarian neoplasms. Clin Cancer Res 2003;9:6453–60.
[30] Gure AO, Chua R, Williamson B, et al. Cancer-testis genes are coordinately expressed and are markers of poor outcome in non small cell lung cancer. Clin Cancer Res 2005;11:8055–62.
[31] Akcakanat A, Kanda T, Tanabe T, et al. Heterogeneous expression of GAGE, NY-ESO-1, MAGE-A and SSX proteins in esophageal cancer: implications for immunotherapy. Int J Cancer 2006;118:123–8.
[32] Fujita S, Wada H, Jungbluth AA, et al. NY-ESO-1 expression and immunogenicity in esophageal cancer. Clin Cancer Res 2004;10:6551–8.
[33] Iura K, Maekawa A, Kohashi K, et al. Cancer-testis antigen expression in synovial sarcoma: NY-ESO-1, PRAME, MAGEA4, and MAGEA1. Hum Pathol 2016;61:130–9.
[34] Rodolfo M, Luksch R, Stockert E, et al. Antigen-specific immunity in neuroblastoma patients antibody and T-cell recognition of NY-ESO-1 tumor antigen. Cancer Res 2003;63:6948–55.
[35] Nicholaou T, Eber L, Davis ID, et al. Directions in the immune targeting of cancer: lessons learned from the cancer-testis Ag NY-ESO-1. Immunol Cell Biol 2006;84:303–17.
[36] Cho H, Caballero OL, Gnjatic S, et al. Physical interaction of two cancer-testis antigens, MAGE-C1 (CT7) and NY-ESO-1 (CT6). Cancer Immun 2006;6:12.
[37] Hayes SJ, Hng KN, Clark P, et al. Immunohistochemical assessment of NYESO-1 expression in esophageal adenocarcinoma resection specimens. World J Gastroenterol 2014;20:4011–6.
[38] Cronwright G, Le Blanc K, Gotherstrom C, et al. Cancer/testis antigen expression in human mesenchymal stem cells: down-regulation of SSX impairs cell migration and matrix metalloproteinase 2 expression. Cancer Res 2005;65:2207–15.
[39] Yawata T, Nakai E, Park KC, et al. Enhanced expression of cancer testis antigen genes in glioma stem cells. Mol Carcinog 2010;49:532–44.