Clinica Chimica Acta 486 (2018) 168–176

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

Review

Prognostic significance of STIP1 expression in human cancer: A meta-analysis

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ARTICLE INFO

Keywords:
Stress-induced protein 1
Overall survival
Disease-free survival
Cancer
Prognosis
Meta-analysis

ABSTRACT

Background: The prognostic significance of stress-induced protein 1 (STIP1) expression in human cancer has been explored in several studies, however, consensus has not been reached. This meta-analysis aimed to summarize the prognostic value of STIP1 expression in cancer.

Methods: Four common databases were searched to seek relevant studies. The meta-analysis was performed to explore the prognostic value of STIP1 expression in overall survival (OS) and clinicopathological parameters in cancer.

Results: Nine studies containing 1417 cancer patients were finally included into the meta-analysis. The results showed the prevalence of high STIP1 expression was 0.50 in patients with cancer. Compared to patients with low expression of STIP1, patients with high STIP1 expression tended to have shorter OS [hazard ratio (HR) = 2.15, 95% confidence interval (CI) = 1.68–2.76, $P < 0.01$]. The subgroup analysis also observed the association between high STIP1 expression and shorter OS in gastrointestinal cancer (HR = 2.02, 95%CI = 1.52–2.69, $P < 0.01$). The online database cross-validation containing 9502 patients also indicated high STIP1 expression predicted shorter OS (HR = 1.40, $P < 0.01$) and disease-free survival (DFS) (HR = 1.30, $P < 0.01$) compared with low STIP1 expression in cancer. Besides, high STIP1 expression was obviously related to earlier lymph node metastasis ($P < 0.01$) and more advanced clinical stage ($P < 0.01$) compared with low STIP1 expression in cancer.

Conclusion: High STIP1 expression was significantly associated with shorter OS, earlier lymph node metastasis and more advanced clinical stage compared with low STIP1 expression in cancer. Therefore, STIP1 expression might be used as a prognostic biomarker for cancer treatment.

1. Introduction

Cancer has become a critical public problem, which accounts for approximately 13% of deaths worldwide [1, 2]. Despite the great advancement of diagnosis and treatment, the prognosis of most cancer cases remains disappointing [3]. In view of this situation, a growing number of researchers begin to seek ideal factors to predict the prognosis of cancer [4–8].

Stress-induced protein 1 (STIP1), also refers to heat shock protein (HSP) 70/HSP90-organizing protein, was initially reported as an auxiliary partner molecule or a scaffold protein [9]. STIP1 modulates the function of HSP by changing the dimmer structure [9]. STIP1 contains three tetratricopeptide repeat (TPR) domains, which interact with HSP to make up complexes [10]. These complexes participate in diverse biological processes, including RNA splicing, transcription, protein folding and cell cycle regulation [11, 12]. Recently, many studies observed dysregulated expression of STIP1 and found STIP1 expression might play an important role in the tumorigenesis, invasion and metastasis of cancer [13–15]. Although previous investigations have explored the prognostic value of STIP1 expression in human cancer [16–24], the association between STIP1 expression and prognosis of cancer remains unclear in several aspects, such as clinical stage and tumor differentiation. Therefore, the aim of this meta-analysis was to evaluate the prognostic significance of STIP1 expression in cancer.

Abbreviations: STIP1, stress-induced protein 1; HSP, heat shock protein; TPR, tetratricopeptide repeat; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; OS, overall survival; DFS, disease-free survival; PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; NOS, Newcastle-Ottawa Scale; GEPIA, Gene Expression Profiling Interactive Analysis; OR, odds ratio; IHC, immunohistochemical; ELISA, enzyme-linked immunosorbent assay; HCC, hepatocellular carcinoma; ESCC, esophageal squamous cell carcinoma

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https://doi.org/10.1016/j.cca.2018.07.037
Received 14 June 2018; Received in revised form 20 July 2018; Accepted 20 July 2018
Available online 01 August 2018
0009-8981/

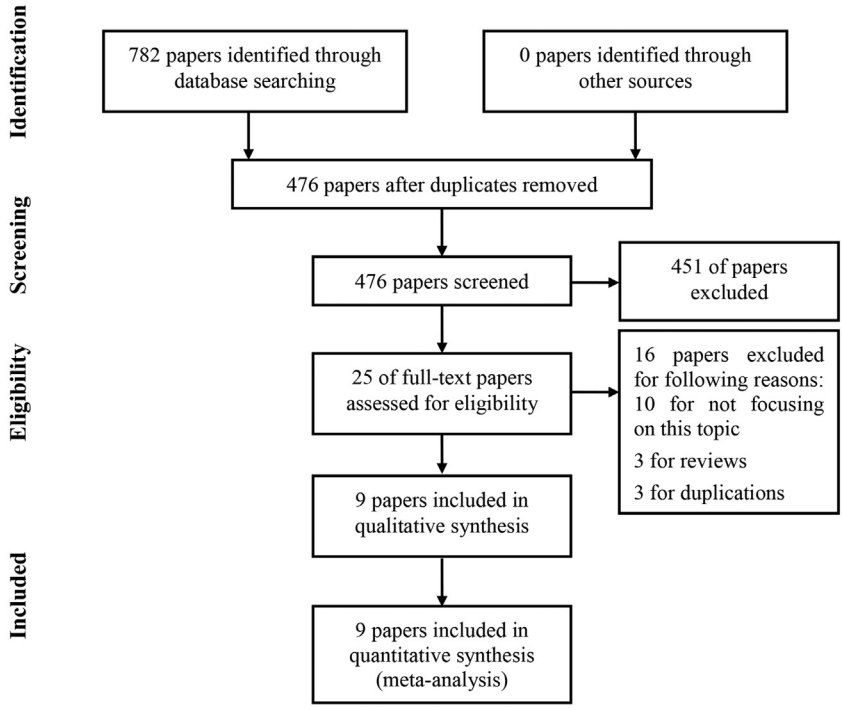

Fig. 1. The flow chart of literature search and selection.

Table 1
The characteristics of included studies.

Study	Patients (n)	STIP1 expression	Clinical stage	Detection methods	Cancer	Main treatment	Outcomes	Analysis	NOS
	(M/F/T)	High/Low	(I + II/III + IV)						
Chao et al. [16]	0/330/330	211/119	183/147	IHC staining	Ovarian Cancer	Surgery	CP,OS,PFS	M	8
Chen et al. [17]	205/26/231	150/81	179/52	IHC staining	HCC	Surgery	CP,OS	M	8
Cho et al. [18]	0/113/113	59/54	34/79	IHC staining	Ovarian Cancer	Surgery	CP,OS	M	8
He et al. [19]	NA/NA/117	44/73	NA	IHC staining	Gastric cancer	NA	OS	U	7
Xu et al. (1) [20]	114/34/148	62/86	42/106	ELISA	ESCC	NA	CP	NA	6
Xu et al. (2) [20]	38/22/60	24/36	13/47	ELISA	ESCC	NA	CP	NA	6
Yang et al. [21]	9/45/54	30/24	NA	IHC staining	Thyroid cancer	Surgery	CP	NA	6
Yuan et al. [22]	34/79/113	62/51	89/24	IHC staining	Thyroid cancer	Surgery	CP,OS	U	7
Zhang et al. [23]	25/82/107	71/36	76/31	IHC staining	Thyroid cancer	Surgery	CP	NA	6
Zhang et al. [24]	88/56/144	60/84	79/65	IHC staining	Colorectal cancer	Surgery	CP,OS,DFS	M	8

M, male; F, female; T, total; STIP1, stress-induced phosphoprotein1; IHC, immunohistochemical; ELISA, enzyme-linked immunosorbent assay; HCC, hepatocellular carcinoma; ESCC, esophageal squamous cell carcinoma; CP, clinicopathological parameter; OS, overall survival; PFS, progression-free survival; DFS, disease-free survival; M, multivariate; U, univariate; NOS, Newcastle-Ottawa Scale; NA, not available.

2. Materials and methods

We performed this study according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [25].

2.1. Literature search and selection

PubMed, Cochrane Library, Web of Science and Embase were comprehensively searched up to May 6th, 2018. The subject terms and search strategy were as follows: ("stress-induced phosphoprotein1" OR "STIP1" OR "HSP70-organizing protein" OR "Hsp70-organizing protein" OR "HOP") AND ("cancer" OR "tumor" OR "neoplasm") AND ("prognosis" OR "predict"). We also checked the references of retrieved articles to avoid missing relevant studies. The literature search and selection were completed by two authors independently. Any disagreement would be solved by group discussion.

2.2. Inclusion criteria and exclusion criteria

The inclusion criteria were as follows: (1) cancer diagnosed by pathological examinations; (2) containing clinical cohorts; (3) focusing on STIP1 expression in cancer prognosis; (4) patients divided into two groups based on the expression level of STIP1; (5) providing overall survival (OS), disease-free survival (DFS), progression-free survival (PFS) or clinicopathological parameters; (6) sufficient data to extract. Reviews, letters, case reports, duplicates, cell experiments, animal experiments and studies without sufficient data were excluded from this research.

2.3. Data extraction and quality assessment

Data extraction and quality assessment were completed by two authors independently. Any disagreement would be solved by group discussion. The following items were extracted from included studies: name of first author, number of patients, gender of patients, number of patients in high STIP1 expression group, detection method of STIP1