Galectins for Diagnosis and Prognostic Assessment of Human Diseases: An Overview of Meta-Analyses

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An increasing number of studies have explored the activities and functions of galectins. However, translation of these researches into clinical practice seems to be lacking. As compared to scattered individual studies, meta-analyses can provide a more comprehensive review of current evidence and reach a more unbiased and powered conclusion by synthesizing data from diverse studies. In this paper, findings from meta-analyses were reviewed to establish the role of galectins in diagnosis and prognostic assessment of various human diseases. First, in patients with cancer, galectin-1 expression is often associated with poorer survival, but galectin-9 expression is associated with better survival. Galectin-3 is a diagnostic biomarker for thyroid cancer and a predictor of worse survival in patients with colorectal cancer and improved survival in patients with gastric cancer. Second, galectin-3 is useful for diagnosis and prognostic assessment of heart failure and prediction of atrial fibrillation and its recurrence. Third, in chronic kidney disease, galectin-3 is valuable for predicting poor survival. Fourth, during pregnancy, galectin-13 is potentially helpful for identifying patients who do not have preeclampsia.

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Background

In 1994, galectins were recognized as a distinct family of beta-galactoside-binding lectins [1]. Today, at least 15 members of the galectin family have been identified, all of which contain carbohydrate-recognition domains (CRDs) in charge of carbohydrate binding [2]. Galectins are classified into three main groups according to their structural features: 1) prototype galectins, which have a single CRD, and include galectins –1, 2, 5, 7, 10, 11, 13, and 14; 2) tandem repeat galectins, which have two distinct CRDs, and include galectins 4, 6, 8, 9, and 12; and 3) chimeric galectins, which have tandem repeats of proline- and glycine-rich short stretches fused onto the CRD, and include galectin-3.

Galectin family members have their respective biological behaviors and functions. Experimental studies have shown that galectins function both intracellularly and extracellularly, and are involved in modulation of cell activation, proliferation, apoptosis, adhesion, migration, and inflammation [3–5]. In addition, clinical evidence has demonstrated the importance of galectins in diagnosis and prognostic assessment of cancer [6], cardiovascular disease (CVD) [7], nephropathies [8], skin diseases [9], and diet-induced steatohepatitis [10].

Meta-analysis, through which data are analyzed after systematic collection from relevant studies, can avert potential reporting bias from a single small sample study, and therefore, may reach a more reliable conclusion [11]. Herein, we have summarized current findings of meta-analyses on clinical use of galectins in various human diseases. This work is potentially worthwhile for researchers to clarify evidence that has been widely published about galectins which could potentially be translated into clinical practice and to identify issues about galectins that have been insufficiently and rarely explored.

Material and Methods

First, we systematically searched the PubMed database on April, 2020 on the terms "(galectin) AND (meta-analysis)". All eligible papers reported results of meta-analyses regarding the role of galectins in clinical diagnosis and assessment of any human disease. Narrative reviews, experiment studies, and single original studies were excluded. Initially, 41 papers were identified, and 25 meta-analyses were finally included. The role of galectins has been studied in meta-analyses only in cancer, CVD, kidney disease, and pregnancy (Figure 1).

Second, we reviewed all eligible papers and recorded which member(s) of the galectin family was/were explored, which type(s) of diseases was/were evaluated, and which outcome(s) of interest was/were analyzed. Overall survival (OS), cancer-specific survival (CSS), relapse-free survival/progression-free
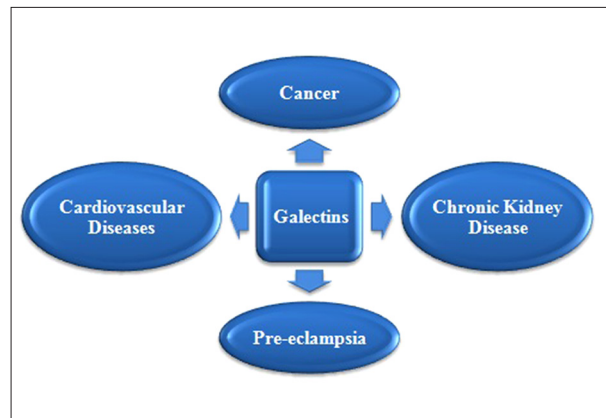

Figure 1. Use of galectins in diagnosis and prognostic assessment of various human diseases based on the results of meta-analyses.

survival (RFS/PFS), and disease-free survival/recurrence-free survival (DFS/RFS) are the main parameters for assessing cancer prognosis and tumor size, stage, and metastasis are the main parameters for assessing the clinicopathological characteristics of cancer.

We also reviewed the effect sizes reported in all included studies. Hazard ratio (HR), odds ratio (OR), risk ratio (RR), and mean difference (MD) were employed to evaluate the association of galectins with survival and clinicopathological data of diseases; and area under the curve (AUC), diagnostic odds ratio (DOR), sensitivity, and specificity were employed to evaluate the accuracy of galectins in diagnosis and prognostic assessment of diseases.

Finally, we reviewed the main findings and conclusions. If two or more meta-analyses focused on the same scientific question, but had different findings, we compared the difference in the number of included papers and quality of the included studies, and also reevaluated the accuracy of statistical methods employed by each meta-analysis, if necessary.

Cancer

Overall, 12 meta-analyses evaluated the role of galectins in diagnosis and assessment of cancer (Table 1). They included various cancers (n=2), solid tumors (n=3), thyroid cancer alone (n=4), pancreatic cancer alone (n=1), gastric cancer alone (n=1), and colorectal cancer alone (n=1). Members of the galectin family evaluated included galectin-1, -3, -4, -8, and -9.

Various cancers

Two different study groups conducted similar meta-analyses to explore the relationship between galectin-1 expression and

Table 1. Evidence from meta-analyses regarding clinical use of galectins in cancer.

First author	Journal (Year)	Regions	No. studies (Pts.)	Galectins studied	Diseases studied	Outcomes of interests	Effect sizes	Conclusions
Wu R	Cancer Cell Int (2018)	China Jiangsu	18 (2674)	Galectin-1 in tissue	Various cancers	Overall survival	Hazard ratio	A significant association between high expression of galectin-1 and poor overall survival
Huang MY	J Cell Physiol (2019)	China Guangdong	29 (3543)	Galectin-1	Various cancers	Cancer-specific survival Overall survival Disease-free survival Progression-free survival Clinicopathologic characteristics	Hazard ratio Odds ratio	A significant association between high expression of galectin-1 and poor overall survival, cancer-specific survival, disease-free survival, and progression-free survival. A significant association between high expression of galectin-1 and larger tumor size, advanced clinical stage, and poorer differentiation
Wang K	Cell Physiol Biochem (2018)	China Jiangsu	14 (2408)	Galectin-9 in tissue	Solid tumors	Cancer-specific survival Overall survival Relapse/progression-free survival	Hazard ratio	A significant association between high expression of galectin-9 and improved cancer-specific survival, but no significant association between galectin-9 expression and overall survival or relapse/progression-free survival
Zhou X	Front Physiol (2018)	China Beijing	14 (2326)	Galectin-9 in tissue	Solid tumors	Overall survival Disease/recurrence-free survival Clinicopathologic characteristics	Hazard ratio Odds ratio	A significant association between high expression of galectin-9 and improved overall survival, a smaller depth of invasion, an earlier histopathological stage, negative lymph node metastasis and negative distal tumor metastasis, but no significant association between galectin-9 expression and disease/recurrence-free survival
Wang Y	Cancer Cell Int (2018)	China Jiangsu	36 (NA)	Galectin-3 in tissue or serum	Solid tumors	Overall survival Disease/progression/recurrence-free survival	Hazard ratio	A significant association between high expression of galectin-3 and reduced overall survival and disease/progression/recurrence-free survival
Xin Y	Int J Clin Exp Pathol (2017)	China Zhejiang	22 (3626)	Galectin-3 (source of specimen is unclear)	Papillary thyroid carcinoma	Diagnosis	Area under the curve Diagnostic odds ratio Sensitivity Specificity	Galectin-3 has an important diagnostic value for papillary thyroid carcinoma
Tang W	Onco Targets Ther (2016)	China Jiangsu	9 (424)	Galectin-3 in tissue	Papillary thyroid carcinoma	Diagnosis Lymph node metastasis	Odds ratio	Galectin-3 may become a potentially useful immunomarker to distinguish papillary thyroid carcinoma Positive galectin-3 expression is more prone to lymph node metastasis in papillary thyroid carcinoma
Trimboli P	Int J Mol Sci (2017)	Switzerland Bellinzona	52 (NA)	Galectin-3 in tissue	Thyroid cancer	Diagnosis	Sensitivity Specificity	There is a high reliability of galectin-3 for thyroid cancer at histology

Table 1 continued. Evidence from meta-analyses regarding clinical use of galectins in cancer.

First author	Journal (Year)	Regions	No. studies (Pts.)	Galectins studied	Diseases studied	Outcomes of interests	Effect sizes	Conclusions
de Matos L	Diagn Pathol (2012)	Brazil São Paulo	39* (5168) 14# (1785)	Galectin-3 in tissue	Thyroid cancer	Diagnosis	Area under the curve Diagnostic odds ratio Sensitivity Specificity	Galectin-3 is accurate in pre- and postoperative diagnosis of benign and malignant thyroid lesions
Sun Q	Cancer Cell Int (2019)	China Shanghai	11 (1227)	Galectin-1, -3, -4, -9 in tissue	Pancreatic cancer	Diagnosis Overall survival Disease-free survival Clinicopathologic characteristics	Area under the curve Diagnostic odds ratio Sensitivity Specificity Hazard ratio Odds ratio	Galectin-3 has a diagnostic value for pancreatic cancer A significant association between high expression of galectin-1 and poorer overall survival A significant association between high expression of galectin-4 and -9 and improved overall survival and disease-free survival No significant association of galectin-3 expression with overall survival and clinicopathologic characteristics
Long B	Int J Surg (2018)	China Gansu	8 (2093)	Galectin-1, -3, -8, -9 in tissue	Gastric cancer	Overall survival Clinicopathologic characteristics	Hazard ratio Odds ratio	A significant association of high galectin-1 expression with poorer overall survival A significant association of low galectin-3, -8, and -9 expressions with poorer overall survival A significant association of high galectin-1 expression with larger tumor size and positive expression of vascular endothelial growth factor A significant association of low galectin-1 expression with lymphatic vessel invasion, worse TNM stage, deeper invasive depth and worse differentiation
Wang C	Pathol Res Pract (2019)	China Xinjiang	15 (1661)	Galectin-3 in tissue or serum	Colorectal cancer	Overall survival Clinicopathologic characteristics	Hazard ratio Odds ratio	A significant association of galectin-3 positive expression with poorer overall survival A significant association of galectin-3 positive expression with advanced TNM stage, higher Duke's stage, venous invasion and higher carcino-embryonic antigen level

NA – not available. * Immunohistochemistry technique; # immunocytochemistry technique.

prognosis in patients with various cancers. Wu R et al. systematically identified 18 studies with 2674 patients, and found that high galectin-1 expression should predict an increased risk of mortality [12]. More recently, Huang M et al. also performed a meta-analysis of 29 studies with 3543 patients, and similarly showed a statistically significant association of high galectin-1 expression with poorer OS (HR=2.12), DFS (HR=1.60), CSS (HR=1.82), and PFS (HR=1.93) [13]. These findings should be cautiously interpreted, because they were produced for unclassified cancer, but not specific to a particular type of cancer.

Solid tumors

Two different study groups conducted similar meta-analyses in 2018 to explore the association of galectin-9 expression with prognosis in patients with solid tumors [14,15]. However, their

conclusions were a bit different. Wang K et al. included 14 studies with 2408 patients up to June 2017, and demonstrated no significant association of high galectin-9 expression with OS (HR=0.80, P=0.311) or RFS/PFS (HR=0.58, P=0.097) in spite of its significant association with better CSS (HR=0.48, P<0.001) [14]. By contrast, Zhou X et al. included 14 studies with 2326 patients up to October 2017, and reported a statistically significant association of high galectin-9 expression with better OS (HR=0.70, P=0.006), rather than DFS/RFS (HR=0.85, P=0.527) [15]. This difference between the two meta-analyses should be discussed. Although the meta-analysis by Wang K et al. included fewer studies than that by Zhou X et al. to explore the association of galectin-9 expression with OS (7 versus 12) [14,15], a further review of studies included in the two meta-analyses suggested that the meta-analysis by Wang K et al., rather than that by Zhou X et al., clearly distinguished CSS from OS. Considering a potential discrepancy between the two outcomes of interests, a conservative conclusion drawn by Wang K et al. should be more reasonable.

Zhou X et al. also reported a significant association of high galectin-9 expression with better clinicopathological characteristics of solid tumors, including less invasion and absence of lymph node or distal tumor metastasis [15].

Wang Y et al. also evaluated the association of galectin-3 with outcomes of solid tumors, and found a statistically significant association of high galectin-3 expression with poorer OS (HR=1.79) and DFS/PFS/RFS (HR=1.57) [16].

Thyroid cancer

Four different study groups performed similar meta-analyses to evaluate the role of galectin-3 in diagnosis of thyroid cancer [17–20]. According to the effect sizes, meta-analyses by de Matos L et al. [17], Xin Y et al. [18], and Trimboli P et al. [19] calculated the sensitivity and specificity to evaluate the diagnostic performance of galectin-3, but the meta-analysis by Tang W et al. calculated the OR to compare the difference in positive galectin-3 expression rate between patients with and without thyroid cancer [20]. Regardless, all of them supported the diagnostic value of galectin-3. Notably, Xin Y et al. also explored the role of Hector Battifora mesothelial antigen-1 in the diagnosis of thyroid cancer and suggested that the AUC of Hector Battifora mesothelial antigen-1 should be larger than that of galectin-3.

Tang W et al. reported a higher rate of positive galectin-3 expression in patients with thyroid cancer who had lymph node metastasis than those without lymph node metastasis [20].

Pancreatic cancer

A meta-analysis by Sun Q et al. included 11 studies to explore the role of galectins in diagnosis and prognostic assessment of pancreatic cancer [21]. They found that galectin-3 had diagnostic value for pancreatic cancer. In addition, high galectin-1 expression and low galectin-4 and galectin-9 expression were significantly associated with poorer OS in pancreatic cancer, but galectin-3 expression was not significantly associated with OS or clinicopathological characteristics.

Gastric cancer

Long et al. systematically identified eight studies involving 2093 patients with gastric cancer [22]. Among them, two studies explored the association between galectin-1 expression and OS, and a meta-analysis further suggested a statistically significant relationship between high galectin-1 expression and poorer OS (HR=1.85, P<0.001). By comparison, four, one, and one studies explored the association of galectin-3, -8, and -9 expressions with OS, respectively; and there were statistically significant associations of high galectin-3 (HR=0.49, P<0.001), galectin-8 (HR=0.35, P<0.001), and galectin-9 (HR=0.78, P=0.003) expressions with better OS.

The meta-analysis also found a significant correlation of high galectin-1 expression with worse clinicopathological characteristics, including larger tumor size, higher TNM stage, presence of lymphatic vessel invasion, and poorer tumor differentiation.

Colorectal cancer

A meta-analysis by Wang C et al. included 15 studies with 1661 patients to explore the association of galectin-3 with OS and clinicopathological features of colorectal cancer [23]. The meta-analysis found statistically significant associations of galectin-3 expression with poorer OS (HR=1.77, 95%CI=1.36-2.31, P<0.0001) and worse clinicopathological features, including higher tumor stage and venous invasion.

Cardiovascular Disease

Overall, seven meta-analyses evaluated the role of galectins in diagnosis and assessment of cardiovascular diseases (Table 2). They included heart failure (n=4), atrial fibrillation (n=2), and ischemic stroke (n=1). The galectin family members evaluated included galectin-2 and -3.

Heart failure

In terms of diagnosis, Huang Z et al. identified eight studies and conducted a meta-analysis on diagnostic value of galectin-3 for heart failure [24]. The pooled AUC, DOR, sensitivity, and specificity of galectin-3 for diagnosis of heart failure were 0.89, 18.29, 81%, and 63%, respectively.

Table 2. Evidence from meta-analyses regarding clinical use of galectins in cardiovascular diseases.

First author	Journal (Year)	Regions	No. studies (Pts.)	Galectins studied	Diseases studied	Outcomes of interests	Effect sizes	Conclusions
Chen H	Heart Fail Rev (2019)	China Zhejiang	18 (7057)	Circulating galectin-3	Acute heart failure	All-cause mortality Cardiovascular mortality Heart failure re-hospitalization	Risk ratio	A significant association between higher serum galectin-3 and higher risks of all-cause mortality and cardiovascular mortality in acute heart failure patients No significant association between higher serum galectin-3 and heart failure rehospitalization
Huang Z	Herz (2018)	China Guangdong	8 (6995)	Galectin-3	Heart failure	Diagnosis	Area under the curve Diagnostic odds ratio Sensitivity Specificity	The diagnostic accuracy of galectin-3 for heart failure is relatively good
Imran T	Am J Cardiol (2017)	USA New Jersey	18 (32350)*	Galectin-3	Heart failure	All-cause mortality Cardiovascular mortality	Hazard ratio	Elevated plasma galectin-3 is significantly associated with a higher risk of all-cause mortality and cardiovascular mortality of heart failure patients
Chen Y	Biomark Med (2016)	China Taiwan	22 (6995)	Galectin-3	Acute and chronic heart failure	All-cause mortality	Area under the curve Diagnostic odds ratio Sensitivity Specificity	Elevated levels of galectin-3 can significantly predict all-cause mortality of heart failure patients
Chen A	Int J Cardiol (2015)	China Shanghai	11 (8419)	Galectin-3	Heart failure	All-cause mortality Cardiovascular mortality	Hazard ratio	A significant association between increased levels of galectin-3 and increased risk of all-cause mortality and cardiovascular mortality
Gong M	J Clin Lab Anal (2020)	China Tianjin	28 (10830)	Galectin-3	Atrial fibrillation Persistent atrial fibrillation	Presence Risk of development Risk of recurrence	Mean difference Odds ratio Hazard ratio	Galectin-3 is significantly associated with atrial fibrillation and persistent atrial fibrillation Galectin-3 can predict both atrial fibrillation development and recurrence after treatment
Pranata R	Indian Pacing Electrophysiol J (2020)	Indonesia Tangerang	7 (597)	Galectin-3	Atrial fibrillation post-ablation	Recurrence post-ablation	Mean difference Hazard ratio	Serum galectin-3 is associated with an increased risk of atrial fibrillation recurrence post-ablation
Zhang G	Cardiovasc Ther (2019)	China Beijing	7 (645)	Circulating galectin-3	Atrial fibrillation patients undergoing catheter ablation	Risk of recurrence	Mean difference Risk ratio	A significant association between higher preprocedural galectin-3 level and increased risk of atrial fibrillation recurrence in patients undergoing catheter ablation
Li W	Atherosclerosis (2010)	China Beijing	7 (21097)	Galectin-2-encoding gene (LGALS2) -C3279T gene polymorphism	Coronary artery disease	Risk of development	Odds ratio	No significant association between LGALS2 -C3279T gene polymorphism and coronary artery disease

Table 2 continued. Evidence from meta-analyses regarding clinical use of galectins in cardiovascular diseases.

First author	Journal (Year)	Regions	No. studies (Pts.)	Galectins studied	Diseases studied	Outcomes of interests	Effect sizes	Conclusions
Misra S	Meta Gene (2016)	India New Delhi	2 (2025)	Galectin-2-encoding gene (LGALS2) -C3279T gene polymorphism	Ischemic stroke	Risk of development	Odds ratio	No significant association between LGALS2 -C3279T gene polymorphism and ischemic stroke

* Studies included heart failure patients and general population.

In terms of prognostic assessment, three different study groups performed similar meta-analyses to evaluate the role of galectin-3 for assessing outcomes of heart failure [25–27]. But they employed different statistical methods and calculated different effect sizes. In 2015, Chen A et al. included 11 studies and found a positive association of galectin-3 with all-cause mortality by using combining categorical (HR=1.30) and continuous (HR=1.28) data [25]. They also found a statistically significant association of galectin-3 with cardiovascular mortality (HR=1.59). In 2016, Chen Y et al. conducted meta-analyses in chronic heart failure (9 studies) and acute heart failure (4 studies) [26]. The pooled AUC, DOR, sensitivity, and specificity of galectin-3 for predicting all-cause death were 0.64, 2.36, 60%, and 61% in chronic heart failure and 0.64, 2.30, 64%, and 57% in acute heart failure, respectively. In 2017, Imran T et al. found a statistically significant association of elevated plasma galectin-3 level with higher risk of all-cause death (HR=1.09) in nine studies and CVD (HR=1.44) in five studies [27]. Taken together, all three meta-analyses indicated that galectin-3 negatively influenced outcomes of heart failure, but its ability might be relatively weak.

Atrial fibrillation

A meta-analysis by Gong M et al. explored the relationship of galectin-3 with risk of atrial fibrillation [28]. They found a significantly higher galectin-3 concentration in patients with atrial fibrillation than those without (MD=-0.268ng/mL) and a significantly higher galectin-3 concentration in patients with persistent atrial fibrillation than those with paroxysmal atrial fibrillation (MD=-0.94ng/mL).

Three different study groups performed similar meta-analyses to evaluate the relationship of galectin-3 with recurrence of atrial fibrillation [28–30]. Two of them found that patients with recurrence of atrial fibrillation had a significantly higher galectin-3 concentration than those without [28,29], but another did not find such a statistically significant difference in galectin-3 concentration between patients with and without recurrence of atrial fibrillation [30]. By comparison, all of them showed that a higher galectin-3 concentration was significantly related to recurrence of atrial fibrillation.

Coronary artery disease

A meta-analysis by Li W et al. identified seven studies involving 10 552 cases and 10 545 controls to evaluate the association of galectin-2-encoding gene (LGALS2) with risk of coronary artery disease [31]. But there was no significant association between them.

Ischemic stroke

Misra S et al. conducted a meta-analysis of two case-control studies to evaluate the association of LGALS2 with risk of ischemic stroke [32]. But there was no significant association between them.

Chronic Kidney Disease

A meta-analysis by Zhang T et al. included five studies with 5 226 patients and evaluated the association of galectin-3 with outcomes of chronic kidney diseases (CKD) [33]. They found that galectin-3 level positively influenced risks of all-cause death (HR=1.379) and cardiovascular events (HR=1.054).

Pregnancy

Three meta-analyses evaluated the diagnostic value of galectins alone or in combination with pulsatility index for preeclampsia (Table 3) [34–36].

Two different study groups published similar meta-analyses in 2015 to explore the diagnostic accuracy of galectin-13 alone for preeclampsia [34,35]. Wu P et al. identified nine studies exploring the role of galectin-13, also known as placental protein 13, for diagnosis of preeclampsia [34]. The AUC was 0.882, sensitivity 37%, and specificity 88%. In another meta-analysis by Zhong Y et al., the sensitivity and specificity of galectin-13 were 47% and 89% for early preeclampsia, 60% and 78% for early preeclampsia, 36% and 90% for small for gestational age, and 51% and 88% for preterm delivery, respectively [35].

Table 3. Evidence from meta-analyses regarding clinical use of galectins in pregnancy.

First author	Journal (Year)	Regions	No. studies (Pts.)	Galectins studied	Diseases studied	Outcomes of interests	Effect sizes	Conclusions
Wu P	Int J Mol Sci (2015)	UK Hartshill	9 (NA)	Galectin-13	Preeclampsia	Diagnosis	Area under the curve Diagnostic odds ratio Sensitivity Specificity	Galectin-13 has a diagnostic value for preeclampsia
Zhong Y	BMC Pregnancy Childbirth (2015)	China Hunan	13 (60786)	Galectin-13	Early preeclampsia Preeclampsia Small for gestational age Preterm delivery	Diagnosis	Sensitivity Specificity	Galectin-13 has a diagnostic value for early preeclampsia, preeclampsia, small for gestational age, and preterm delivery
Zhu X	Ann Med (2015)	China Shanghai	4 (NA)	Galectin-13	All preeclampsia Early preeclampsia Late preeclampsia	Diagnosis	Sensitivity	Galectin-13 combined with uterine artery pulsatility index exhibits a relatively good predictive ability for early preeclampsia, but a poor predictive ability for late preeclampsia

NA – not available.

Both meta-analyses suggested a high specificity (i.e., true negative rate) for galectin-13, but low sensitivity (i.e., true positive rate).

Zhu X et al. evaluated diagnostic performance of galectin-13 in combination with uterine artery pulsatility index for all, early, and late preeclampsia [36]. The sensitivities were 69%, 77%, and 54%, respectively. These findings suggested that galectin-13 in combination with uterine artery pulsatility index had a relatively good diagnostic ability for early preeclampsia, but not for late pre-eclampsia.

Conclusions

The current work, which reviews well-established evidence from meta-analyses, is valuable for investigators to avoid duplicate studies, guide clinical translation of research, and explore untouched issues associated with galectins in future. Several major findings regarding the clinical usefulness of galectins in various human diseases can be summarized as follows.

1. Galectin-1 expression negatively influences survival of patients with cancer; by contrast, galectin-9 expression may be a protective factor for better outcomes in such patients.

Galectin-3 has good diagnostic value for thyroid cancer. However, the prognostic value of galectin-3 is entirely converse between patients with gastric cancer and those with colorectal cancer. Galectin-3 expression may be a risk factor for survival in colorectal cancer, but a protective factor in gastric cancer. Galectin-3 expression is not associated with the outcomes of pancreatic cancer.

2. Galectin-3 level may be valuable for screening for heart failure and assessing its outcomes. However, its ability in assessing the outcomes is relatively weak in such patients. Galectin-3 level is increased with both development and recurrence of atrial fibrillation. Additionally, LGALS2 has no significant impact on the risk of coronary artery disease or ischemic stroke.

3. Galectin-3 level has a negative impact on the outcome of CKD.

4. Galectin-13 level is relatively accurate for identifying patients without a diagnosis of preeclampsia, but has very limited value for identifying true positive cases.

Notably, the clinical importance of other members of the galectin family in these diseases has not been fully studied by meta-analyses. In addition, clinical use of galectins in other human diseases needs to be further explored.

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