Clin. Lab. 2023;69:XXX-XXX

REVIEW ARTICLE

De Ritis Ratio: a Potent Marker in Cancer

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SUMMARY

Background: **The role of conventional liver function clinical laboratory marker De Ritis Ratio in evaluating the prognosis, assisting diagnosis, and monitoring therapeutic efficacy of cancer is gaining increasing attention, especially in the last decade. According to the most recent articles, the De Ritis Ratio functions have progressed, which indicates that the De Ritis Ratio appears to be a promising tumor marker. The aim of this review was to evaluate the clinical importance from studies made on this subject.**
Methods: **Using the search words "De Ritis Ratio", "aspartate transaminase/alanine transaminase", "aspartate transaminase", "alanine transaminase", "cancer", "prognostic significance", "diagnostic significance", and "predictive significance", a search was carried out on PubMed. Exclusion criteria were articles never published in English and articles evaluating tumor markers in cancer not involving the De Ritis Ratio.**
Results: **As a predictor of prognosis, the De Ritis Ratio is strongly associated with prognostic risk factors and can be used to assess therapeutic efficacy. As a predictor of incidence, the De Ritis Ratio could promote the prediction of the disease progression. As a biomarker, the De Ritis Ratio is more likely to improve diagnostics by being combined with other biomarkers. Therefore, since it is easily accessible, involves no additional laborious efforts, and is a relatively inexpensive marker, the De Ritis Ratio is emerging as an attractive and clinically valuable marker in cancer.**
Conclusions: **In the review, we explore the possible mechanisms of the De Ritis Ratio related to cancer and summarize the clinical importance of the De Ritis Ratio as a promising marker for cancer.**
(Clin. Lab. 2023;69:xx-xx. DOI: 10.7754/Clin.Lab.2023.230528)

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Review Article accepted June 16, 2023

Supplementary Data

Table S1. Evaluation of the De Ritis Ratio as prognostic marker in cancers.

Author year	Study design	Pts. No.	Parameters evaluated	Types of cancer	Cut-off level	follow-up time/ over survival	HR/p-value (univariate analysis)	HR/p-value (multivariate analysis)
Changchien et al. [5] 2008	R	6,381	De Ritis Ratio, HBsAg, AFP	HCC	NA	1-year/44.3% 3-year/ 24.9% 5-year/17.1% 7-year/13%	NA	NA
Bezan et al. [39] 2015	R	698	De Ritis Ratio	RCC	1.26	8-year 88.5%	NA	1.76/< 0.001
Lee et al. [40] 2017	R	1,547	De Ritis Ratio	localized RCC	1.5	73-month/NA	NA	1.770/0.002
Ghahari et al. [41] 2022	R	89	De Ritis Ratio	BC	1.3	4-year/64.3%	3.11/< 0.001	3.09/0.01
Varol et al. [42] 2020	R	191	De Ritis Ratio, NLR	advanced PC	0.75	50-month/4.7%	NA	NA
Ikeda et al. [43] 2020	R	243	De Ritis Ratio	ESRD-associated RCC	1.42	NA	NA	NA
Ishihara et al. [44] 2017	R	118	De Ritis Ratio	mRCC	1.24	NA	1.83/0.0921	2.3/0.0258
Li et al. [45] 2019	R	908	De Ritis Ratio	localized UTUC	1.23	58-month/ 47.4%	1.925/ < 0.001	1.842/< 0.001
Shen et al. [46] 2021	R and P	1,490	De Ritis Ratio, HBV-DNA	HBV-related HCC	1	5-year/ type 1:69.8% type 2:59.2% type 3:50.5% type 4:42.7%	2.327/ < 0.001	1.574/0.001
Cho et al. [47] 2017	R	1,049	De Ritis Ratio	UUTUC	1.6	64-month/ 72.2%	2.17/0.001	1.84/0.001
Knittelfelder et al. [48] 2020	R	515	De Ritis Ratio	OOSCC	1.44	61-month/ 61.9%	1.69/< 0.001	1.42/0.002
Guner et al. [49] 2020	R	171	De Ritis Ratio	TC	1.35	NA	NA	NA
Fukui et al. [50] 2021	NA	138	De Ritis Ratio	NMIBC	1.35	NA	NA	5.558/0.01
Yuk et al. [51] 2019	NA	771	De Ritis Ratio	BUC	1.1	NA	NA	2.15/0.007
Lee et al. [52] 2017	R	623	De Ritis Ratio	UTUC	1.5	26-month/ 23.7%	NA	2.164/< 0.001
Nishikawa et al. [53] 2016	R	109	De Ritis Ratio	UUTUC	1.3	5-year/56.8%	4.12/< 0.001	4.21/< 0.001
Cheng et al. [54] 2021	R	314	De Ritis Ratio	NMIBC	1.4	3-year/NA	NA	NA

Table S1. Evaluation of the De Ritis Ratio as prognostic marker in cancers (continues).

Author year	Study design	Pts. No.	Parameters evaluated	Types of cancer	Cut-off level	follow-up time/ over survival	HR/p-value (univariate analysis)	HR/p-value (multivariate analysis)
Kang et al. [55] 2020	R	670	De Ritis Ratio	RCC	Preoperative: 1.0 Postoperative:	81-month/ 83.9%	2.41/0.002	2.18/0.008
Scheipner et al. [56] 2021	R	536	De Ritis Ratio	CRC	0.96	5-year/ 81.6%	1.4/0.14	1.24/0.35
Zhang et al. [57] 2019	R	414	De Ritis Ratio, GGT	HCC	1.26	5-year/ 50.5%	1.698/0.000	1.424/0.017
Wang et al. [58] 2019	R	438	De Ritis Ratio, PSA	localized PCa	1.325	low ratio group: 2-year/97.2% 5-year/86.1% high ratio group: 2-year/93.7% 5-year/69.3%	2.385/ < 0.001	1.718/0.027
Canat et al. [59] 2019	R	298	De Ritis Ratio	localized RCC	1.5	54-month/NA	NA/0.456	NA
Gorgel et al. [60] 2019	R	128	De Ritis Ratio	TC	1.30	NA	NA	NA
Ha et al. [61] 2019	R	118	De Ritis Ratio	BC	1.3	NA	NA	2.761/0.001
Li et al. [62] 2020	R	190	nomogram model (age, clinical stage De Ritis Ratio)	GC	1.24	5-year/63.2%	1.699/0.034	1.758/0.024
Gu et al. [63] 2017	R	185	nomogram model (histological subtype, system invasion, metastasis at surgery, De Ritis Ratio, albumin)	RCC and VTT		NM patients: 1-year/90.5% 3-year/68.1% 5-year/52.0% M patients: 1-year/67.5% 3-year/58.9% 5-year/40.0%	2.002/0.009	2.492/0.012

P - prospective, R – retrospective, NA - not available for evaluation, HCC - hepatocellular carcinoma, HBsAg - hepatitis B surface antigen, AFP - α-fetoprotein, RCC - renal cell carcinoma, Type 1 - HBV-DNA ≤ 103 IU/mL and AST/ALT ≤ 1, Type 2 - HBV-DNA ≤ 103 IU/mL and AST/ALT > 1, Type 3 - HBV-DNA > 103 IU/mL and AST/ALT ≤ 1, Type 4 - HBV-DNA >103 IU/mL and AST/ALT > 1, mRCC - metastatic renal cell carcinoma, ESRD - end-stage renal disease, PC - pancreatic cancer, OOSCC - oral and oropharyngeal squamous cell cancer, TC - testicular cancer, UTUC - upper tract urothelial cancer, CRC - colorectal cancer patients, GC - gastric cancer, NMIBC - high-risk non-muscle invasive bladder cancer, PCa - prostate cancer, BUC - bladder urothelial carcinoma, PSA - prostate-specific antigen, BC - bladder cancer, UUTUC - upper urinarytract urothelial carcinoma, NLR - neutrophil/lymphocyte ratio, VTT - venous tumor thrombus, NM patients - non-metastaticpatients, M patients - metastatic patients.