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Review

Usefulness of Nutrition and Inflammation Assessment Tools in Esophageal Cancer Treatment

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Abstract. *Multidisciplinary treatment for esophageal cancer leads to nutritional and inflammatory changes. Recent studies showed that nutritional and inflammatory changes during multidisciplinary treatment affect both short and long-term oncological outcomes in esophageal cancer treatment. Therefore, evaluation of the nutritional and inflammatory status during treatment is necessary in order to optimize and utilize multidisciplinary therapy for esophageal cancer. If patients with esophageal cancer are able to determine their nutritional and inflammatory status, they will be able to select the optimal esophageal cancer, anti-inflammation, and nutritional treatments. Various types of nutrition and inflammation assessment tools have been developed and reported for esophageal cancer, with each tool having its own clinical characteristics, which must be understood before being applied in clinical practice. This review summarizes the background, current status, and future perspectives on the application of nutrition and inflammation assessment tools in esophageal cancer treatment.*

Esophageal cancer is the eighth most common type of cancer and the sixth-leading cause of cancer-related death in the world (1, 2). Curative resection and perioperative adjuvant treatment is a standard treatment for resectable esophageal cancer (3-5). Although the survival rate after surgery and adjuvant treatment is gradually increasing, almost half of all patients develop recurrent disease, even after curative treatment (6, 7).

Recently, some studies have reported that the perioperative nutritional and inflammatory status affect both the short-term and long-term oncological outcomes in various malignancies (8, 9). Therefore, it is necessary to evaluate the nutritional and inflammatory status during the perioperative period in patients with esophageal cancer. If a physician can determine the nutritional and inflammatory status during treatment, they can control and manage the nutritional and inflammatory status to optimize esophageal cancer treatment. Thus far, the application of various nutritional and inflammation assessment tools, such as the Glasgow Prognostic Score (GPS), Prognostic Nutritional Index (PNI), and Controlling Nutritional Status (CONUT) have been reported in esophageal cancer (10-14). To introduce these various nutritional and inflammation assessment tools into daily clinical practice, it is necessary to understand the characteristics of each.

This review summarizes the background, current status, and future perspectives of nutrition and inflammation assessment tools in esophageal cancer treatment.

Search Strategy

The search strategy used in the current study was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A literature search was performed on PubMed. The following keywords were used: "Glasgow Prognostic Score (GPS)" and "esophageal cancer (or carcinoma)"; "Prognostic Nutritional Index" and "esophageal cancer (or carcinoma)"; "Controlling Nutritional Status" and "esophageal cancer (or carcinoma)"; "neutrophil-lymphocyte

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ratio (NLR)" and "esophageal cancer (or carcinoma)." "CRP to albumin ratio (CAR)" and "esophageal cancer (or carcinoma)"; "platelet-to-lymphocyte ratio (PLR)" and "esophageal cancer (or carcinoma)"; "albumin-to-globulin ratio (AGR)" and "esophageal cancer (or carcinoma)"; and "lymphocyte-to-C-reactive-protein ratio (LCR)" and "esophageal cancer (or carcinoma)". In addition, the references of the cited articles were overlooked. In total, 920 articles were identified. However, 782 were excluded.

Clinical Use of the GPS and Modified GPS (mGPS) in Esophageal Cancer Treatment

The GPS is calculated using the serum C-reactive protein level (CRP) and serum albumin level (15). Both CRP and albumin are produced by the liver. The serum CRP level reflects the systemic inflammation status, and the serum albumin level reflects the nutritional status. Therefore, the GPS can assess both the inflammatory and nutritional status during treatment. The mGPS has also been investigated and reported in various malignancies. A total of 29 studies have evaluated the clinical impact of the GPS/mGPS in esophageal cancer, using a cut-off value of 1 or 2. Table I summarizes each study (16-44). Among them, 21 studies evaluated patients with esophageal cancer who underwent esophagectomy, four evaluated patients who received chemotherapy, four evaluated patients who received chemoradiation therapy, one evaluated patients who received radiation therapy, and one evaluated patients who underwent esophageal stent insertion. All studies demonstrated that a high GPS/mGPS (GPS/mGPS >1 or 2) was associated with a poor prognosis. The hazard ratio (HR) of a high GPS/mGPS for OS was 1.367-5.62 in the surgery group, 1.51-2.151 in the chemotherapy group, and 1.694-2.528 in the chemoradiation group. Accordingly, the GPS/mGPS had a clinical impact on the oncological outcomes in esophageal cancer, irrespective of the treatment method. Further studies are needed to clarify whether the GPS/mGPS has a clinical impact on short-term oncological outcomes (*e.g.*, occurrence of postoperative surgical complications, continuation of chemotherapy/radiation therapy, and occurrence of chemotherapy/radiation therapy toxicity).

The CRP to Albumin Ratio (CAR) in Esophageal Cancer Treatment

The CAR is derived from laboratory tests and is determined by dividing the serum CRP level by the albumin level. The CAR evaluates both the inflammatory status and the nutritional status. Thirteen studies evaluated the clinical impact of CAR in esophageal cancer. Table II summarizes each study (45-56). Among them, 12 studies evaluated CAR as a prognostic factor and one study evaluated it as a predictive factor for postoperative surgical complications. All studies showed that a high CAR was associated with a poor oncological outcome. In the evaluation as a prognostic factor, 10 studies evaluated patients with esophageal cancer who underwent esophagectomy, one study evaluated patients who received chemotherapy, and one study evaluated patients who received chemoradiation therapy. The reported cut-off values of CAR as a prognostic factor in these studies ranged from 0.0139 to 0.5. Among the patients who underwent esophagectomy, the HR of a high CAR for OS was 1.393-3.02. Further studies are needed to clarify whether the CAR is an optimal tool for unresectable esophageal cancer.

The Neutrophil-to-Lymphocyte Ratio (NLR) in Esophageal Cancer Treatment

The NLR is determined by dividing the absolute neutrophil count by the absolute lymphocyte count. Recent studies demonstrated that a high NLR is associated with a poor prognosis in various malignancies. Thus far, 63 studies have evaluated the clinical impact of the NLR in esophageal cancer. Table III summarizes each study (57-93). Thirty-eight studies evaluated the NLR as a prognostic factor. Among them, 26 evaluated patients with esophageal cancer who underwent esophagectomy, five evaluated patients who received chemoradiation therapy, three evaluated patients who underwent chemotherapy, and three evaluated patients who received combined treatment. All studies demonstrated that a high NLR was associated with a poor prognosis. The reported cut-off values of the NLR as a prognostic factor ranged from 1.77 to 6.4 in these studies. The HR of the NLR for OS was 1.129-5.445 in the surgery group, 2.5-6.31 in the chemotherapy group, and 1.597-2.357 in the chemoradiation group. Accordingly, the NLR has a clinical impact on the oncological outcomes in esophageal cancer, irrespective of the treatment method.

The Platelet-to-Lymphocyte Ratio (PLR) in Esophageal Cancer Treatment

Recently, the PLR was reported as a promising prognostic factor for gastrointestinal malignancies. The PLR is calculated by dividing the platelet count by the lymphocyte count. Eleven studies evaluated the clinical impact of the PLR in esophageal cancer. Table IV summarizes each study (94-103). Among them, 10 evaluated the PLR as a prognostic factor, while one study evaluated the PLR as a predictive factor for postoperative surgical complications. The cut-off value of the PLR as a prognostic factor was reported to be 73-192 in these studies. In studies that evaluated the PLR as a prognostic factor, a high PLR was associated with a poor prognosis. The HR of the PLR for OS was 1.37-2.475. Although the PLR showed prognostic

Table I. *Literature investigating the utility of the Glasgow Prognostic Score (GPS)/modified Glasgow Prognostic Score (mGPS) in patients with esophageal cancer.*

First author	Ref	Year	Country	Tool	Tumor stage	Sample size	Treatment	Cut-off value	Endpoint	HR	95% CI	Research duration
Crumley	16	2006	UK	GPS	IV	258	Chemotherapy	1 and 2	OS	1.51	1.22-1.86	2000-2004
Crumley	17	2007	UK	GPS	IV	65	Chemotherapy	1 and 2	OS	1.65	1.1-2.47	1999-2005
Kobayashi	18	2008	Japan	GPS	II-III	48	Surgery	1	OS	0.17	0.06-0.52	2000-2007
Crumley	19	2010	UK	mGPS	I-III	217	Surgery	1 and 2	OS	1.67	1.35-2.07	2002-2004
Kobayashi	20	2010	Japan	GPS	I-III	65	Surgery	1	OS	0.071	0.011-0.470	1999-2007
Vashist	21	2011	Germany	GPS	I-IV	495	Surgery	1 and 2	OS	1.7	1.3-2.2	1994-2007
Crumley	22	2011	UK	mGPS	I-IV	100	Surgery	1	OS	3.99	1.96-8.11	1996-2004
Dutta	23	2011	UK	GPS	I-III	121	Surgery	1 and 2	CSS	1.96	1.09-3.54	2005-2009
Dutta	24	2011	UK	mGPS	I-IV	112	Surgery	1 and 2	CSS	4.32	2.20-8.45	1996-2008
Dutta	25	2012	UK	mGPS	I-III	121	Surgery	1 and 2	CSS	2.91	1.51-5.62	1996-209
Nakamura	26	2014	Japan	mGPS	I-IV	168	Surgery	2	OS	2.726	1.021-7.112	2003-2008
Feng	27	2014	China	GPS	I-III	493	Surgery	1 and 2	CSS	1.907	1.608-2.262	2005-2008
Morikawa	28	2014	Japan	GPS	IV	278	Chemotherapy	1 and 2	OS	0.61	0.46-0.81	2007-2011
Zhang	29	2014	China	GPS	I-IV	212	Chemoradiotherapy	1	OS	1.694	1.350-2.126	2006-2011
Feng	30	2014	China	GPS	I-III	375	Surgery	1	OS	1.367	1.114-1.677	2006-2008
Hirahara	31	2015	Japan	GPS	I-III	141	Surgery	1	OS	2.045	1.032-3.928	2006-2014
Ohira	32	2015	Japan	GPS	II, III	91	Chemotherapy + surgery	1	OS	2.151	1.167-3.966	2000-2013
Liu	33	2015	China	GPS	I-III	326	Surgery	1	CSS	1.438	1.176-1.759	2006-2008
Kimura	34	2016	Japan	GPS	III, IV	142	Chemoradiotherapy	2	CSS	2.528	1.494-4.277	2002-2011
Ma	35	2016	China	GPS	I-III	725	Surgery	1	OS	1.625	1.155-2.286	2006-2010
Ikeguchi	36	2016	Japan	GPS	III, IV	68	Surgery	1	OS	3.554	1.161-10.878	2004-2014
Lindenmann	37	2017	Austria	GPS	I-III	174	Surgery	1	OS	2.17	1.28-3.69	2003-2011
Okuno	38	2017	Japan	GPS	IV	142	Chemoradiotherapy	2	OS	1.95	1.19-3.18	2000-2006
Driver	39	2018	UK	GPS	IV	209	Esophageal stent insertion	1 and 2	OS	2.4	1.5-3.8	2009-2013
Yu	40	2018	China	mGPS	I	160	Surgery	1	OS	0.068	0.007-0.662	2005-2012
Wu	41	2018	Taiwan	mGPS	III	63	Surgery	1	OS	3.13	1.66-5.88	2005-2015
Sugawara	42	2018	Japan	GPS	I-III	47	Surgery	1	OS	5.62	1.94-16.4	2006-2016
Tsuchiya	43	2022	Japan	GPS	III	155	Radiation therapy	1	OS	2.26	1.11-4.60	2000-2018
Cui	44	2022	Chia	mGPS	I-IV	311	Surgery	1	OS	3	1.751-4.369	2012-2018

CI: Confidence interval; CSS: cancer-specific survival; HR: hazard ratio; (m)GPS: (modified) Glasgow Prognostic Score; OS: overall survival.

Table II. *Literature investigating the utility of the C-reactive protein-to albumin-ratio in patients with esophageal cancer.*

First author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Xu	45	2015	China	I-III	468	Surgery	0.5	OS	2.44	1.82-3.26	2000-2010
Wei	46	2015	China	I-IV	423	Surgery	0.095	OS	1.393	1.031-1.883	2006-2010
Otowa	47	2017	Japan	II, III	149	Surgery	0.048	OS	0.298	0.174-0.503	2007-2014
Kudou	48	2018	Japan	I-III	144	Surgery	0.1	OS	2.378	1.025-5.249	2005-2016
Ishibashi	49	2018	Japan	I-III	143	Surgery	0.085	OS	1.994	1.153-3.501	2009-2014
Yu	40	2018	China	I	160	Surgery	0.023	OS	0.126	0.017-0.911	2005-2012
Kunizaki	50	2018	Japan	I-IV	116	Surgery	0.042	OS	2.35	1.189-4.650	2007-2014
Zhang	51	2019	China	I-III	266	Chemoradiation	0.13	OS	4.344	3.145-5.999	2012-2014
Tamagawa	52	2020	Japan	I-III	122	Surgery	0.04	OS	2.401	1.208-4.770	2005-2018
Sakai	53	2020	Japan	I-IV	105	Surgery	0.026	OS	2.69	1.19-6.06	2006-2014
Sugimoto	54	2021	Japan	I-IV	295	Surgery	0.0139	AL	3.02	1.01-9.06	2007-2020
Ishibashi	55	2021	Japan	I-IV	171	Surgery	0.088	OS	1.663	1.016-2.764	2009-2016
Inoue	56	2022	Japan	IV	41	Chemotherapy	0.119	OS	10.149	2.664-66.729	2020-2022

AL: Anastomotic leakage; CI: Confidence interval; CAR: C-reactive protein-to albumin-ratio; HR: hazard ratio; OS: overall survival.

Table III. *Literature investigating the utility of the neutrophil-to-lymphocyte ratio for overall survival in patients with esophageal cancer.*

First author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	HR	95% CI	Research duration
Yoo	57	2014	Korea	II, III	138	Chemoradiotherapy	2	2.115	1.193-3.749	2005-2010
Yuan	58	2014	China	I-IV	327	Surgery	5	2.743	2.073-3.630	2009-2012
Yutong	59	2015	China	I-IV	820	Surgery	3.5	1.287	1.049-1.580	2007-2008
Duan	60	2015	China	I-III	371	Surgery	3	1.591	1.132-2.235	2000-2007
Xiao	61	2016	China	I-III	121	Surgery	1.77	2.03	1.262-3.264	2007-2014
Jung	62	2016	Korea	I-III	119	Surgery	2.35	1.23	No data	2004-2012
Kosumi	63	2016	Japan	I-IV	283	Surgery	1.94	1.84	1.17-3.18	2005-2010
Ji	64	2016	China	I-III	41	Surgery	5	2.86	1.01-8.12	2009-2012
Gao	65	2017	China	I-IV	1,281	Surgery	2.86	1.892	1.567-2.284	2005-2015
Zhang	66	2017	China	II, III	355	Surgery	3.5	2.303	1.617-3.280	2010-2011
Conway	67	2017	UK	II-IV	316	Mix	3	1.48	1.09-2.03	2009-2015
Zhou	68	2017	China	II-IV	517	Chemoradiotherapy	5	1.856	1.498-2.300	2006-2010
Nakamura	69	2017	Japan	T1	245	Surgery	2.42	2.76	1.50-5.03	2005-2016
He	70	2017	China	I-IV	317	Surgery	3.3	1.36	1.015-1.840	2000-2010
Xu	71	2018	China	I-III	419	Surgery	2.998	No data	1.35-3.95	2010-2012
Ishibashi	72	2019	Japan	I-IV	85	Surgery	3.84	0.52	0.296-0.920	2009-2014
Li	73	2019	China	I-III	204	Chemoradiotherapy	2.64	1.597	1.151-2.215	2010-2014
Guo	74	2019	Taiwan	IV	49	Chemotherapy	6.4	6.31	2.38-16.77	2015-2017
Chen	75	2019	Taiwan	I-IV	1,168	Mix	3	1.49	1.30-1.69	2007-2018
Guo	76	2020	China	I-III	103	Surgery	2.5	1.129	1.034-1.232	2010-2014
Shang	77	2020	China	I-IV	1,883	Surgery	2.06	1.247	1.024-1.519	2005-2015
Sugawara	78	2020	Japan	-	378	Surgery	2.57	1.95	no data	2006-2016
Powell	79	2020	UK	I-III	136	Surgery	2.25	2.26	1.03-3.08	2010-2018
Sakin	80	2021	Turkey	I-III	80	Surgery	2.8	5.445	2.081-4.547	2008-2018
Zheng	81	2021	China	I-III	167	Surgery	2.2	1.47	1.033-2.093	2017-2020
Kato	82	2021	Japan	I-III	121	Surgery	1.9	2.195	1.103-4.367	2010-2015
Peng	83	2021	China	I-III	121	Surgery	2.24	2.366	1.024-5.464	2013-2017
Ho	84	2021	Taiwan	II, III	101	Chemoradiotherapy	3.56	2.357	1.357-4.004	2010-2015
Hoshino	85	2021	Japan	IV	133	Mix	3.374	1.061	1.002-1.125	2004-2019
Gao	86	2021	China	I-III	2,542	Surgery	3	1.236	1.069-1.430	2009-2014
Koh	87	2021	Korea	I-III	68	Chemoradiotherapy	4.77	1.818	1.043-3.168	2006-2017
Wang	88	2021	China	II, III	113	Surgery	2.07	2.47	1.550-3.936	2014-2019
Powell	89	2021	UK	I-III	294	Surgery	2.5	2.66	1.58-4.50	2004-2018
Guo	90	2021	China	I-III	278	Surgery	3	3.426	2.528-4.641	2010-2013
Gao	91	2022	China	I-IV	140	Chemotherapy	5	4.01	2.28-7.06	2016-2021
Wang	92	2022	China	IV	69	Chemotherapy	4	2.5	1.33-4.68	2016-2018
Ohsawa	93	2022	Japan	I-IV	163	Surgery	4.5	3.88	2.38-6.32	2003-2018

CI: Confidence interval; HR: hazard ratio.

value in esophageal cancer treatment, most studies assessed patients who underwent esophagectomy. Therefore, further studies are needed to clarify the clinical impact of the PLR in patients who receive chemotherapy or chemoradiation therapy.

The PNI in Esophageal Cancer Treatment

The PNI is a novel index that is used to assess the immune and nutritional status based on the serum lymphocyte count and albumin level. Twenty-six studies evaluated the clinical impact of the PNI in esophageal cancer. Table V summarizes each study (104-126). Among the 23 studies that evaluated the PNI as a prognostic factor, 13 evaluated patients with esophageal cancer who underwent esophagectomy, three evaluated patients who underwent endoscopic submucosal dissection, one evaluated patients who received chemotherapy, and six studies evaluated patients who received combined treatment. The cut-off value of the PNI as a prognostic factor in these studies was reported to range from 35.93 to 54.15. All studies demonstrated that a low PNI was associated with a poor prognosis. The HR of the PNI for OS was 1.186-2.92 in the surgery group and 1.69-2.42 in the endoscopic submucosal dissection group. Accordingly, the PNI had a clinical impact on the oncological outcomes in esophageal cancer, irrespective of the treatment method.

Table IV. *Literature investigating the utility of the platelet-to-lymphocyte ratio in patients with esophageal cancer.*

First author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Messaer	94	2015	UK	I-III	153	Surgery	192	OS	2.47	1.21-5.01	2001-2014
Yang	95	2018	China	I-III	515	Surgery	133	OS	1.37	1.076-1.745	2005-2011
Chen	96	2019	China	I-III	107	Surgery	150	OS	2.475	1.458-4.203	2001-2012
Wang	97	2019	China	I-IV	73	Mix	73	OS	1.751	1.042-2.945	2009-2017
Gao	98	2019	China	I-III	468	Surgery	117.05	OS	1.37	1.067-1.758	2005-2008
Zhang	99	2019	China	I-IV	2,469	Surgery	94.68	OS	1.39	1.21-1.60	2000-2010
Han	100	2020	China	I-III	379	Chemoradiation	153	Esophageal fistula	2.359	1.096-5.080	2015-2018
Cai	101	2020	China	I-III	311	Surgery	142.17	OS	1.74	1.24-2.46	2012-2014
Wang	88	2021	China	II-III	113	Surgery + chemoradiation	183.06	OS	2.431	1.560-3.789	2014-2019
Aoyama	102	2022	Japan	I-III	168	Surgery	150	OS	1.553	10.26-2.350	2005-2018
Kato	103	2022	Japan	I-III	174	Surgery	169.6	OS			2010-2015

CI: Confidence interval; HR: hazard ratio.

CONUT in Esophageal Cancer Treatment

The CONUT score was developed as an accessible nutritional screening tool for evaluating patients' nutritional status. The CONUT score is calculated from the serum albumin level, the total cholesterol level, and the total lymphocyte count. The clinical impact of the CONUT score on the outcomes of esophageal cancer was first reported in 2016. Eight studies evaluated the clinical impact of the CONUT in esophageal cancer. Table VI summarizes each study (127-133). Among them, six studies evaluated the CONUT score as a prognostic factor and two evaluated it as a predictive factor for postoperative surgical complications. Six studies showed that a high CONUT score was associated with a poor oncological outcome. In the studies that evaluated the CONUT score as a prognostic factor, five studies evaluated esophageal cancer patients who received esophagectomy, and one study evaluated patients who received chemotherapy. The reported cut-off values of the CONUT score as a prognostic factor ranged from 1 to 5 in these studies. Among the patients who underwent esophagectomy, the HR of a high CONUT score for OS was 1.23-3.56.

The Albumin-to-Globulin Ratio (AGR) and the Lymphocyte-to-C-reactive Protein Ratio (LCR) in Esophageal Cancer Treatment

Recently, the clinical utility of albumin and globulin as tumor prognostic markers have aroused great interest, due to the close relationship with the nutritional status and the inflammatory responses of cancer patients. The AGR, which is calculated as AGR = albumin/(total protein–albumin) has been considered a possible effective combination of the two individual prognostic indicators. In addition, the lymphocyte-to-C-reactive-protein ratio (LCR) is a particularly promising marker of systemic inflammation in the perioperative period. Table VII and Table VIII showed the clinical impact of the AGR and LCR in esophageal cancer treatment (134-138). However, limited studies have shown its significance as a prognostic factor in esophageal cancer treatment. Additional studies are needed to clarify the clinical impact of the AGR and LCR in esophageal cancer treatment.

Future Prospects for Nutrition and Inflammation Assessment Tools in Esophageal Cancer Treatment

Thus far, various nutrition and inflammation assessment tools have been applied in esophageal cancer treatment. To utilize the nutrition and inflammation assessment tools in esophageal cancer treatment, the following points should be clarified. Firstly, setting the optimal cut-off value of each tool is an issue. In the previous studies, patient background factors and treatment methods were heterogeneous. In addition, the sample sizes of the previous studies were relatively small, and the studies were retrospective in nature. Therefore, these differences may have affected the cut-off values of each tool. In addition, the timing at which each tool should be applied is also unclear. It remains necessary to establish the optimal timing for assessment by these tools. Secondly, the mechanisms through which nutrition and inflammation affect the prognosis of esophageal cancer are unclear. Recently, the nutritional and inflammatory status was reported to affect postoperative surgical complications, the introduction of chemotherapy, and adverse events of chemotherapy. However, the precise mechanism through which the nutritional and inflammatory status, as assessed by these tools, influence the prognosis of esophageal cancer is unclear. Thirdly, it is unclear whether these nutrition and inflammation assessment tools

Table V. *Literature investigating the utility of the Prognostic Nutritional Index for overall survival in patients with esophageal cancer.*

First author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	HR	95% CI	Research duration
Feng	104	2013	China	I-III	375	Surgery	42	2.558	1.718-3.809	2006-2008
Nakatani	105	2017	Japan	II, III	66	Surgery	45	2.92	1.31-6.48	2009-2015
Zhang	106	2018	China	I-III	655	Surgery	54.15	0.777	0.626-0.964	2005-2013
Nakatani	107	2018	Japan	IV	76	Surgery	45	1.75	1.01-3.06	2001-2015
Matsumoto	108	2018	Japan	I-IV	191	Radiotherapy + chemotherapy	43.2	0.93	0.88-0.98	2005-2016
Sakai	109	2018	Japan	I-IV	32	Chemoradiation and surgery	45	0.86	0.77-0.95	1998-2015
Urabe	110	2018	Japan	I-IV	1363	Mix	44.8	0.62	0.47-0.82	1999-2014
Higake	111	2019	Japan	I-IV	141	Surgery	45	1.862	1.112-3.118	2008-2014
Dai	112	2019	China	I-III	106	Radiotherapy + chemotherapy	48.15	0.537	0.342-8.44	2000-2015
Xiao	113	2020	China	II-III	193	Radiotherapy + chemotherapy	47.975	0.584	0.408-0.835	2012-2017
Okadome	114	2020	Japan	I-IV	371	Surgery	45	1.67	1.14-2.44	2005-2014
Qi	115	2021	China	I-IV	407	Surgery	48.33	1.529	1.163-2.011	2010-2014
Kim	116	2021	Korea	IV	60	Chemotherapy	35.93	4.07	1.29-12.90	2016-2019
Fujiwara	117	2021	Japan	I-IV	111	Surgery	44.2	0.292	0.145-0.588	2010-2019
Kubo	118	2021	Japan	I-IV	336	Surgery	45	1.573	1.042-2.347	2011-2017
Suzuki	119	2021	Japan	I	241	ESD	45	2.39	1.28-4.46	2007-2017
Xiao	120	2021	China	I-IV	4,146	Mix	45	1.2	1.05-1.5	2006-2014
Kang	121	2022	China	I-IV	2,661	Surgery	49	1.186	1.012-1.391	2006-2017
Shimada	122	2022	Japan	I-IV	593	ESD	45	1.69	1.08-2.65	2006-2017
Zheng	123	2022	China	I-III	165	Surgery	43.5	0.948	0.907-0.991	2017-2020
Zhao	124	2022	China	I-III	354	Surgery	50.5	0.754	0.577-0.984	2011-2017
Haneda	125	2022	Japan	I-IV	158	Surgery	40.9	2.171	1.249-3.775	2009-2019
Iwai	126	2022	Japan	I	566	ESD	47.75	2.42	1.26-4.65	2007-2015

CI: Confidence interval; ESD: endoscopic submucosal dissection; HR: hazard ratio.

Table VI. *Literature investigating the utility of the Controlling Nutritional Status in patients with esophageal cancer.*

Study	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Toyokawa	127	2016	Japan	I-IV	185	Surgery	3	OS	2.3	1.19-4.45	2000-2014
Yoshida	128	2016	Japan	I-IV	352	Surgery	5	Surgical complications	2.75	1.081-7.020	2005-2014
Yoshida	129	2017	Japan	I-III	373	Surgery	5	OS	3.56	1.71-7.39	2005-2016
Hirahara	130	2018	Japan	I-III	148	Surgery	2	CSS	1.99	1.05-3.78	2002-2014
Hikage	113	2019	Japan	I-IV	141	Surgery	5	OS	2.48	1.33-4.63	2008-2017
Yoon	131	2021	Korea	I-IV	1,265	Surgery	2	OS	1.23	1.140-1.340	2005-2018
Chang	132	2022	China	IV	69	Chemotherapy	1	OS	2.056	1.031-4.098	2017-2020
Horinouchi	133	2022	Japan	I-III	674	Surgery	5	Surgical complications	3.38	1.225-9.332	2005-2021

CI: Confidence interval; HR: hazard ratio; OS: overall survival.

will become promising indicators for treatment approaches targeting nutrition/inflammation in esophageal cancer. The clinical relationship between changes in the nutritional and inflammatory status and perioperative oral nutritional treatment need to be clarified.

Conclusion

The nutritional and inflammatory status, as assessed by nutrition and inflammation assessment tools, may have some clinical influence on both the short-term and long-term

Table VII. *Literature investigating the utility of the albumin-to-globulin ratio in patients with esophageal cancer.*

First author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Li	134	2017	China	I-IV	447	Surgery	1.66	OS	1.32	1.008-1.728	2007-2009
Oki	135	2017	Japan	I-IV	112	Surgery	1.41	DFS	0.18	0.03-0.93	2002-2014
Atsumi	136	2021	Japan	I-III	105	Surgery	1.48	OS	2.27	1.24-4.17	2005-2018

CI: Confidence interval; DFS: disease-free survival; HR: hazard ratio; OS: overall survival.

Table VIII. *Literature investigating the utility of the lymphocyte-to-C-reactive protein ratio for overall survival in patients with esophageal cancer.*

First author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	HR	95% CI	Research duration
Takeichi	137	2021	Japan	IV	495	Chemotherapy	19,000	2.24	1.61-3.12	2000-2019
Yamamoto	138	2021	Japan	I-IV	153	Surgery	7,842	2.76	1.33-5.86	2002-2017

CI: Confidence interval; HR: hazard ratio.

oncological outcomes of patients with esophageal cancer. However, the optimal cut-off values for each tool are unclear, as are the mechanisms through which these parameters influence prognosis. To optimize the nutrition and inflammation assessment tools for patients with esophageal cancer, it is necessary to clarify these points in further studies.

Conflicts of Interest

The Authors have no conflicts of interest to declare.

Authors' Contributions

TA and KK made substantial contributions to the concept and design. TA, YM, KH, and KK made substantial contributions to the acquisition of data and the analysis and interpretation of the data. TA and KK were involved in drafting the article or revising it critically for important intellectual content. TA, YM, and KH gave their final approval of the version to be published.

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