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Review

Clinical Impact of Nutrition and Inflammation Assessment Tools in Gastric Cancer Treatment

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Abstract. *The standard treatment for gastric cancer is surgical resection and perioperative adjuvant treatment. Multidisciplinary treatment for gastric cancer leads to nutritional and inflammatory changes. Nutritional and inflammatory changes during multidisciplinary treatment can lead to poor physical activity, severe toxicity in patients receiving chemotherapy or radiation therapy, and poor oncological outcomes. Evaluation of the perioperative nutritional and inflammatory status during treatment is necessary in order to utilize and optimize multidisciplinary therapy for gastric cancer. If physicians were able to detect the perioperative nutritional and inflammatory status before and during gastric cancer treatment, they would be able to select the optimal treatment and perioperative nutritional treatment. Recently, various types of nutrition and inflammation assessment tools were developed and reported for gastric cancer. These nutrition and inflammation assessment tools have some clinical advantages, such as ease of implementation, perioperative accessibility, and low cost. On the other hand, each tool has its own clinical characteristics, which must be understood before using it in the clinical practice. This review summarizes the background, current status, and future perspectives on the application of nutrition and inflammation assessment tools in gastric cancer treatment.*

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An estimated 19.3 million new cancer cases and 10.0 million cancer deaths occurred worldwide in 2020 (1, 2). Among them, gastric cancer is one of the most frequent types of cancer. Curative resection and perioperative adjuvant treatment is the standard treatment for gastric cancer (3-5). Although the prognosis of patients with gastric cancer is gradually improving, more than half of patients develop recurrent disease, even after curative treatment (6, 7). Thus, in order to improve the prognosis of gastric cancer, it is necessary to identify useful prognostic factors.

Thus far, the perioperative nutritional status and the inflammatory status have been shown to affect short-term oncological outcomes, including postoperative surgical complications, continuation of adjuvant treatment, and adverse events of adjuvant treatment (8-12). In addition, the perioperative nutritional status and inflammatory status affect the long-term oncological outcomes (13, 14). The evaluation of the perioperative nutritional status and the inflammatory status during treatment is necessary for utilizing and optimizing multidisciplinary therapy for gastric cancer. If physicians were able to detect the perioperative nutritional status and inflammatory status before and during gastric cancer treatment, they would be select optimal treatment and perioperative nutritional treatment. Recently, various types of nutrition and inflammation assessment tools for patients with gastric cancer have been developed and reported. The perioperative nutritional assessment of gastric cancer has been based on changes in body composition, blood biochemistry, or a combination of both. These nutrition and inflammation assessment tools have some clinical advantages, including ease of implementation, perioperative accessibility, and low cost. On the other hand, each tool has its own clinical characteristics, therefore it is necessary to understand the characteristics of each nutrition and inflammation assessment tool before using it in clinical practice.

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

Clinical Use of the Glasgow Prognostic Score and Modified Glasgow Prognostic Score in Gastric Cancer Treatment

The Glasgow Prognostic Score (GPS) was first reported by Forrest and McMillan (15). The GPS is determined from the serum C-reactive protein level (CRP) and serum albumin level. The CRP level reflects the systemic inflammation status and the albumin level reflect the nutritional status. Therefore, the GPS can assess both the inflammatory and nutritional status associated with malignancy. The GPS is determined as follows: Cases with both elevated CRP (>10 mg/l) and low albumin (<35 g/l) are scored as 2; cases with only one of these biochemical abnormalities are scored as 1; and cases with neither of these abnormalities are scored as 0. After further investigation, the GPS was modified. The mGPS is scored as follows: Cases with both elevated CRP (>10 mg/l) and low albumin (<35 g/l) are scored as 2; cases with elevated CRP are scored as 1; and cases with neither elevated CRP nor low albumin are scored as 0. A total of 17 studies have evaluated the clinical impact of the GPS/mGPS in gastric cancer. Table I summarizes each study (16-32). In previous studies, the cut-off value of the GPS/mGPS was 1 or 2. Among them, 10 studies evaluated resectable gastric cancer and seven evaluated unresectable gastric cancer. In both the resectable and unresectable settings, a high GPS/mGPS (more than 1 or 2) was associated with a poor prognosis. The hazard ratio (HR) of GPS/mGPS for overall survival (OS) was 1.042-5.07 in the resectable setting and 1.621-5.89 in the unresectable setting. In addition, two studies showed that a high GPS/mGPS was associated with the occurrence of postoperative surgical complications. Accordingly, GPS and mGPS have clinical impact in relation to both the short- and long-term oncological outcomes in gastric cancer.

The C-Reactive Protein-to Albumin-Ratio in Gastric Cancer Treatment

The C-reactive protein to albumin ratio (CRP/Alb) is derived from laboratory tests. The CRP/Alb is determined by dividing the serum CRP level by the albumin level. CRP is an acute-phase response protein synthesized by liver cells and is one of the most sensitive indicators of inflammation. Albumin is synthesized by the liver and is the main component of human serum total protein. Albumin plays an important role in maintaining blood colloid osmotic pressure, transporting metabolites, and reflects the nutritional status. Therefore, the CRP/Alb ratio reflects both the inflammation status and the nutrition status. Thus far, 11 studies have evaluated the clinical impact of CRP/Alb in gastric cancer. Table II summarizes each study (33-43). Among them, nine studies evaluated CRP/Alb as a prognostic factor, while two studies evaluated it as a predictive factor for postoperative surgical complications. The cut-off CRP/Alb value was reported to range from 0.025 to 0.3778 as a prognostic factor in the previous studies. In the evaluation as a prognostic factor, a high CRP/Alb value was associated with a poor prognosis. The hazard ratio (HR) of the CRP/Alb value for OS was 1.626-2.844. In addition, two studies showed that a high CRP/Alb value was associated with the occurrence of postoperative surgical complications. Accordingly, the CRP/Alb value is considered to have a clinical impact on both the short- and long-term oncological outcomes. Further studies are needed to clarify whether CRP/Alb is an optimal tool for unresectable gastric cancer. In other malignancies, recent studies showed that the CRP/Alb ratio is a promising marker for selecting patients who are eligible for chemotherapy or as a predictor of adverse events of chemotherapy. These issues need to be clarified in gastric cancer.

The Neutrophil-to-Lymphocyte Ratio in Gastric Cancer Treatment

The neutrophil-lymphocyte ratio (NLR) was first recognized for its association with systemic inflammation in the critically ill, and meta-analyses on the association between an elevated NLR and a poor prognosis have been reported for various malignancies. The NLR is determined by dividing the absolute neutrophil count by the absolute lymphocyte count. The NLR can easily be calculated from parameters that are obtained in routine blood cell counts. The close association between inflammation and cancer progression hints at the potential application of elevated tumor-associated neutrophils, or neutrophils that infiltrate tumors, as a prognostic biomarker. Thus far, 63 studies have evaluated the clinical impact of NLR in gastric cancer. Table III summarizes each study (18, 44-97). Among them, 60 studies evaluated the NLR as a prognostic factor, three evaluated the NLR as a predictive factor for postoperative surgical complications. Among 60 studies that evaluated the NLR as a prognostic factor, 34 evaluated its role in resectable gastric cancer and 26 studies evaluated unresectable gastric cancer. In both the resectable and unresectable settings, a high NLR was associated with a poor prognosis. The HR of NLR for OS was 1.1-14.621 in the resectable setting and 1.116-11.41 in the unresectable setting. The cut-off value of the NLR was reported to be 1.7-5 in the resectable setting and 1.5-5 in the unresectable setting. In addition, three studies showed that a high NLR was associated with the occurrence of postoperative surgical complications. Accordingly, the NLR had clinical impact in both short- and long-term oncological outcomes in resectable and unresectable settings. Recently, changes of the NLR during treatment have been reported to be associated with gastric cancer survival. Further studies are needed to clarify this issue.

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

Author (Ref)	Year	Country	Type of GPS	Tumor stage	Sample size	Treatment	Cut-off value	Endpoint	HR	95% CI	Research duration
Nozoe *et al*. (16)	2011	Japan	mGPS	I-IV	232	Surgery	2	OS	4.184	1.792-9.804	1998-2008
Kubota *et al*. (17)	2012	Japan	GPS	I-III	1669	Surgery	2	OS	5.07	1.94-11.41	2005-2008
Jeong *et al*. (18)	2012	Korea	mGPS	IV	104	Chemotherapy	1	OS	3.14	1.75-5.61	2002-2009
Kunisaki *et al*. (19)	2012	Japan	GPS	IV	83	Chemotherapy	1	OS	3.446	1.772-6.701	2007-2010
Hwang *et al*. (20)	2012	Korea	GPS	IV	402	Chemotherapy	1	OS	1.79	1.29-2.47	2004-2009
Jiang *et al*. (21)	2012	Japan	GPS	I-IV	1710	Surgery	1	OS	1.845	1.184-2.875	2000-2007
Dutta *et al*. (22)	2012	UK	GPS	I-III	120	Surgery	1	OS	2.23	1.40-3.54	1996-2009
Mimatsu *et al*. (23)	2014	Japan	GPS	IV	36	Surgery	2	OS	0.156	0.049-0.519	2006-2013
Li *et al*. (24)	2014	China	GPS	IV	384	Chemotherapy	1	OS	1.621	1.124-2.339	2004-2011
Ishizuka *et al*. (25)	2014	Japan	GPS	I-IV	650	Surgery	1	OS	2.048	1.002-4.185	2000-2010
Melling *et al*. (26)	2016	Germany	GPS	I-IV	368	Surgery	1	OS	1.6	1.0-2.4	2009-2014
Yuan *et al*. (27)	2017	China	GPS	IV	384	Chemotherapy	1	OS	1.76	1.13-2.73	2006-2014
Hsueh *et al*. (28)	2019	Taiwan	GPS	III	272	Surgery	1	Surgical complications	1.97	1.36-2.86	2007-2014
Kurosaki *et al*. (29)	2020	Japan	GPS	IV	80	Chemotherapy	2	OS	5.89	2.52-23.80	2017-2019
Tokuyama *et al*. (30)	2021	Japan	GPS	IV	45	Chemotherapy	1	OS	3.63	1.73-7.91	2015-2019
Shimoda *et al*. (31)	2021	Japan	GPS	II-III	424	Surgery	1	Surgical complications	1.877	1.039-3.388	2007-2019
Zhang *et al*. (32)	2022	China	mGPS	I-IV	488	Surgery	2	OS	1.042	1.105-1.772	2006-2016

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

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

Author (Ref)	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Liu *et al*. (33)	2015	China	I-III	455	Surgery	0.025	OS	1.626	1.191-2.219	2005-2010
Toiyama *et al*. (34)	2016	Japan	I-III	384	Surgery	0.058	OS	2.21	1.19-4.11	2001-2011
Mao *et al*. (35)	2017	China	I-IV	337	Surgery	0.3778	OS	1.78	1.20-2.65	2010
Saito *et al*. (36)	2018	Japan	I-IV	453	Surgery	0.0232	OS	1.975	1.152-3.386	2005-2013
Xu *et al*. (37)	2019	China	I-III	401	Surgery	0.131	OS	2.108	1.082-4.107	2015-2016
Kudou *et al*. (38)	2019	Japan	I-IV	144	Surgery	0.1	OS	2.378	1.025-5.249	2005-2016
Toyokawa *et al*. (39)	2020	Japan	III	225	Surgery	0.47	OS	2.844	1.561-5.181	1997-2012
Lee *et al*. (40)	2020	Korea	I-III	128	Surgery	0.265	Surgical complications	2.832	1.023-7.841	2016-2019
Yu *et al*. (41)	2021	China	I-IV	205	Surgery	0.07	OS	1.86	1.13-3.01	2015-2019
Aoyama *et al*. (42)	2022	Japan	I-III	481	Surgery	0.05	OS	2.397	1.461-3.934	2013-2017
Liu *et al*. (43)	2022	China	I-III	206	Surgery	2.105	Surgical complications	2.538	1.346-4.785	2015-2017

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

The Platelet-to-Lymphocyte Ratio in Gastric Cancer Treatment

Recently, the platelet-to-lymphocyte ratio (PLR) was developed and reported as a promising prognostic factor for gastrointestinal malignancies. The PLR is particularly promising as it can potentially provide insight into both cancer-related inflammation and cancer-related thrombotic/hemostatic mechanisms in various malignancies. Five studies have evaluated the clinical impact of the PLR in gastric cancer. Table IV summarizes each study (39, 48, 98-100). Among them, four studies 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 159-191 in the previous studies. In evaluation as a prognostic factor, a high PLR was associated with a poor prognosis. The HR of the PLR for OS was 1.552-2.47. Although almost 30 studies have assessed the prognostic value of the PLR in gastric

Table III. *Literature investigating the utility of the neutrophil-to-lymphocyte ratio in patients with gastric cancer.*

Author (Ref)	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Yamanaka *et al*. (44)	2007	Japan	IV	1220	Chemotherapy	2.5	OS	1.52	1.32-1.75	1999-2000
Ubukata *et al*. (45)	2010	Japan	I-IV	157	Surgery	5	OS	5.779	0.950-35.170	1996-2003
Shimada *et al*. (46)	2010	Japan	I-IV	1028	Surgery	4	OS	1.845	1.236-2.747	2001-2007
Jung *et al*. (47)	2011	Korea	III-IV	293	Surgery	2	OS	1.462	1.033-2.068	2004-2007
Jeong *et al*. (18)	2012	Korea	IV	104	Chemotherapy	3	OS	1.65	1.03-2.64	2002-2009
Lee *et al*. (48)	2013	Korea	IV	174	Chemotherapy	3	OS	2.245	2.092-3.633	2007-2010
Cho *et al*. (49)	2014	Korea	IV	268	Chemotherapy	3.06	OS	1.569	1.227-2.006	2006-2009
Qiu *et al*. (50)	2014	China	I-IV	706	Surgery	3	OS	1.544	1.084-2.2	2001-2008
Aziz (51)	2014	Egypt	III-IV	70	Surgery	3	OS	3.259	1.144-9.282	2010-2014
Yuan *et al*. (52)	2014	China	I-IV	327	Surgery	5	OS	2.743	2.073-3.630	2009-2012
Hsu *et al*. (53)	2015	Taiwan	I-IV	1030	Surgery	3.44	OS	1.565	1.198-2.044	2005-2011
Kim *et al*. (54)	2015	Korea	I-III	601	Surgery	1.7	OS	2.12	1.30-3.44	2005-2011
Yu *et al*. (55)	2015	China	I-III	291	Surgery	3.5	OS	0.626	0.460-0.852	2005-2009
Graziosi *et al*. (56)	2015	Italy	I-IV	156	Surgery	2.34	OS	1.7	1.02-2.84	2003-2012
Namikawa *et al*. (57)	2016	Japan	IV	224	Chemotherapy	4	OS	1.651	1.187-2.297	2007-2014
Ock *et al*. (58)	2016	Korea	IV	745	Chemotherapy	2.42	OS	1.56	1.28-1.92	2004-2014
Grenader *et al*. (59)	2016	Israel	IV	392	Chemotherapy	3	OS	1.67	1.45-1.93	2000-2005
Mohri *et al*. (60)	2016	Japan	I-III	404	Surgery	3	Postoperative complications	1.85	1.02-3.35	2000-2011
Wang *et al*. (61)	2016	US	I-IV	1498	Surgery	2.76	DFS	1.1	1.05-1.13	1998-2013
Fanotto *et al*. (62)	2017	Italy	IV	868	Chemotherapy	2.7	OS	0.66	0.53-0.81	2006-2015
Lieto *et al*. (63)	2017	Italy	I-IV	297	Surgery	3.22	OS	3.04	1.20-7.68	2000-2015
Qu *et al*. (64)	2017	China	I-IV	436	Surgery	2.51	OS	2.372	1.170-4.811	2007-2013
Jin *et al*. (65)	2017	China	I-III	119	Surgery	2.23	OS	1.758	1.058-2.217	2004-2011
Ogata *et al*. (66)	2018	Japan	IV	26	Chemotherapy	5	OS	5.38	1.34-21.6	2017
Kim *et al*. (67)	2018	Korea	IV	502	Chemotherapy	3	OS	1.43	1.17-1.73	2007-2013
Hwang *et al*. (68)	2018	Korea	IV	73	Chemotherapy	3	OS	1.795	1.026-3.140	2011-2017
Jung *et al*. (69)	2018	Korea	IV	265	Chemotherapy	5	OS	2.269	-	2015
Gonda *et al*. (70)	2018	Japan	IV	110	Chemotherapy	3	OS	1.493	1.054-2.138	2013-2015
Mori *et al*. (71)	2018	Japan	II/III	100	Surgery	2.6	OS	6.736	2.420-18.748	2006-2017
Ramos-Esquivel *et al*. (72)	2018	Costa Rica	I-IV	381	Surgery	5	OS	2.33	1.73-3.13	2009-2012
Zhang *et al*. (73)	2018	China	I-III	904	Surgery	2	OS	1.257	1.031-1.532	2010-2011
Zhang *et al*. (74)	2018	China	I-IV	182	Surgery	2.88	OS	1.585	1.011-2.485	2011-2014
Szor *et al*. (75)	2018	Brazil	I-III	383	Surgery	2.44	OS	1.5	1.27-4.21	2009-2016
Miyamoto *et al*. (76)	2018	Japan	II, III	154	Surgery	3	OS	1.506	1.047-2.167	1992-2018
Migita *et al*. (77)	2018	Japan	I-IV	167	Surgery	2.2	OS	2.679	1.848-3.884	2001-2015
Zhou *et al*. (78)	2019	China	IV	537	Chemotherapy	2.61	OS	1.448	1.030-2.034	2010-2018
Murakami *et al*. (79)	2019	Japan	IV	92	Chemotherapy	2.83	OS	1.116	1.063-1.171	2006-2017
Inoue *et al*. (80)	2019	Japan	IV	86	Chemotherapy	3	OS	1.845	1.144-2.976	2010-2015
Tanaka *et al*. (81)	2019	Japan	II, III	170	Surgery	1.99	OS	2.51	1.273-4.978	2006-2015
Kim *et al*. (82)	2020	Korea	IV	116	Chemotherapy	2.92	OS	1.77	1.04-3.04	2018-2019
Zhao *et al*. (83)	2020	China	IV	110	Chemotherapy	2.48	OS	1.617	1.032-2.535	2012-2018
Yong *et al*. (84)	2020	China	I-IV	221	Surgery	2.5	Postoperative complications	2.44	1.52-3.68	2015-2018
Li *et al*. (85)	2020	China	II-IV	225	Surgery	2.57	OS	1.176	1.008-1.348	2014-2018
Gou *et al*. (86)	2021	China	IV	137	Chemotherapy	3.23	OS	0.34	0.22-0.52	2016-2020
Ruan *et al*. (87)	2021	China	IV	58	Chemotherapy	2.7	OS	11.41	1.98-65.76	2016-2017
Castineiras *et al*. (88)	2021	Spain	IV	116	Chemotherapy	3.96	OS	2.16	1.29-3.61	2009-2019
Park *et al*. (89)	2021	Korea	IV	112	Chemotherapy	2.81	OS	1.75	1.12-2.71	2011-2018
Yang and Li (90)	2021	China	I-III	147	Surgery	2.8	OS	2.625	1.505-4.186	2015-2019
Mori *et al*. (91)	2021	Japan	I-III	400	Surgery	2.7	Postoperative complications	14.621	1.160-184.348	2006-2019
Sato *et al*. (92)	2021	Japan	IV	121	Surgery	3	OS	1.506	1.047-2.167	1992-2018
Yamakoshi *et al*. (93)	2021	Japan	I-IV	199	Surgery	2.33	OS	1.65	1.068-2.579	2007-2010
Liu *et al*. (94)	2021	China	I-IV	111	Surgery	1.75	OS	1.945	2.180-22.430	2016-2019
Ishido *et al*. (95)	2022	Japan	IV	59	Chemotherapy	1.5	OS	3.127	1.492-6.555	2017-2020
Namikawa *et al*. (96)	2022	Japan	IV	411	Chemotherapy	3.57	OS	3.47	1.174-1.769	2007-2019
Martínez et al. (97)	2022	Spain	I-III	147	Surgery	2.4	OS	1.55	1.0-2.37	1998-2012

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

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

Author (Ref)	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Lee *et al*. (48)	2013	Korea	IV	174	Chemotherapy	160	OS	1.743	1.142-2.847	2007-2010
Messager *et al*. (98)	2015	UK	I-III	153	Surgery	192	OS	2.47	1.21-5.01	2001-2017
Inaoka *et al*. (99)	2017	Japan	I-III	312	Surgery	0.77	Surgical complications	3.32	1.82-6.25	1999-2016
Chen *et al*. (100)	2019	China	I-IV	91	Surgery	162	OS	0.304	0.123-0.752	2008-2015
Toyokawa *et al*. (39)	2020	Japan	III	225	Surgery	172	OS	1.552	1.029-2.341	1997-2012

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

Table V. *Literature investigating the utility of the Prognostic Nutritional Index in patients with gastric cancer.*

Author (Ref)	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Watanabe *et al*. (101)	2012	Japan	I-IV	99	Surgery	44.7	OS	2.692	1.149-6.306	2005-2011
Jiang *et al*. (102)	2014	China	I-III	581	Surgery	46	OS	2.223	1.344-3.676	2003-2008
Sun *et al*. (103)	2015	China	I-IV	632	Surgery	48.2	OS	1.668	1.368-2.035	1998-2008
Lee *et al*. (104)	2016	Korea	I-III	7781	Surgery	46.7	OS	1.383	1.221-1.568	2001-2010
Hirahara *et al*. (105)	2018	Japan	I-III	368	Surgery	44.3	OS	2.794	1.352-6.039	2010-2016
Wang *et al*. (106)	2018	China	III	274	Surgery	46.3	OS	0.46	0.29-0.74	2010-2015
Migita *et al*. (77)	2018	Japan	I-IV	167	Surgery	47	OS	1.821	1.255-2.642	2001-2015
Luo *et al*. (107)	2018	China	II-IV	128	Surgery	50	OS	12.993	5.911-28.560	2014-2017
Park *et al*. (108)	2019	Korea	II, III	1868	Surgery	49.7	OS	0.853	0.822-0.997	2006-2010
Zhang *et al*. (109)	2020	China	I-IV	273	Surgery	41.25	OS	0.782	0.503-0.997	2010-2014
Zhu *et al*. (110)	2020	China	I-IV	245	Surgery	43	CSS	2.351	1.026-3.676	2005-2015
Xiao *et al*. (111)	2020	China	II, III	1288	Surgery	43.9	CSS	1.287	1.058-1.565	2010-2017
Sugawara *et al*. (112)	2020	Japan	I-III	309	Surgery	45	OS	1.6	1.03-2.5	2002-2016
Takechi *et al*. (113)	2020	Japan	I-III	222	Surgery	45	OS	2.889	1.104-7.563	2011-2014
Takahashi *et al*. (114)	2020	Japan	I-III	86	Surgery	46.5	OS	2.15	1.37-3.94	2009-2015
Sasahara *et al*. (115)	2020	Japan	II, III	842	Surgery	47	OS	1.82	1.26-2.64	2010-2014
Watanabe *et al*. (116)	2021	Japan	IV	110	Chemotherapy	40	OS	2.398	1.384-4.154	2015-2019
Sánchez *et al*. (117)	2021	Mexico	I-IV	940	Surgery	41	OS	0.586	0.429-0.801	2005-2018
Demirelli *et al*. (118)	2021	Turkey	IV	87	Surgery	45	OS	4.2	1.73-10.1	2011-2016
Zhang *et al*. (119)	2021	China	I-III	454	Surgery	45.1	OS	1.685	1.120-2.534	2010-2017
Liu *et al*. (120)	2021	China	I-III	191	Surgery	47.77	OS	1.88	1.28-2.78	2008-2018
Okubo *et al*. (121)	2021	Japan	I-III	90	Surgery	49.4	OS	1.695	1.06-2.77	2009-2018
Lee *et al*. (122)	2022	Korea	IV	35	Chemotherapy	40	OS	0.349	0.142-0.860	2017-2021
Konishi *et al*. (123)	2022	Japan	I-III	447	Surgery	48	OS	2.8	1.65-4.78	2008-2013
Xu *et al*. (124)	2022	China	I-III	771	Surgery	48.8	OS	0.614	0.421-0.896	2010-2015

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

cancer, limited studies showed that the PLR had a significant impact for OS in gastric cancer. Therefore, further studies are needed to clarify the clinical impact of the PLR in gastric cancer treatment.

The Prognostic Nutritional Index in Gastric Cancer Treatment

The prognostic nutritional index (PNI) is a novel method to assess the immune and nutritional status based on the serum lymphocyte count and albumin level. Twenty-six studies have evaluated the clinical impact of the PNI in gastric cancer. Table V summarizes each study (77, 101-124). Among the 26 studies that evaluated the PNI as a prognostic factor, 24 evaluated resectable gastric cancer and two evaluated unresectable gastric cancer. In both the resectable and unresectable settings, a high PNI was associated with a poor prognosis. The HR of the PNI for OS was 1.287-12.933 in the resectable setting. The cut-off value of the PNI was reported to be 41-50 in the resectable setting and 40 in the unresectable setting. Recent studies have reported that the immune status and nutritional status affect the continuation of chemotherapy

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

Author (Ref)	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Ryo *et al*. (125)	2018	Japan	II-III	626	Surgery	2	OS	1.97	1.26-2.41	2010-2014
Liu *et al*. (126)	2018	China	II-III	697	Surgery	3	OS	1.553	1.080-2.232	2000-2012
Kuroda *et al*. (127)	2018	Japan	I-III	416	Surgery	4	OS	2.72	1.74-4.25	2005-2014
Hunag *et al*. (128)	2019	China	I-III	357	Surgery	2	OS	2.695	1.631-4.451	2014-2016
Hirahara *et al*. (129)	2019	Japan	I-IV	210	Surgery	3	OS	2.441	1.463-4.071	2010-2016
Suzuki *et al*. (130)	2019	Japan	I-III	261	Surgery	5	OS	2.12	1.18-3.69	2000-2015
Jin *et al*. (131)	2021	China	I-III	272	Surgery	4	OS	1.618	1.111-2.356	2004-2015
Zhu *et al*. (132)	2021	China	I-IV	245	Surgery	3	OS	2.031	1.117-2.945	2005-2015
Sun *et al*. (133)	2021	China	I-III	1479	Surgery	2	Surgical complications	1.156	1.077-1.240	2016-2018
Qian *et al*. (134)	2021	China	I-IV	309	Surgery	2.5	Surgical complications	2.433	1.218-4.862	2016-2019
Chen *et al*. (135)	2022	China	IV	146	Chemotherapy	0	OS	1.697	1.023-2.813	2016-2020
Aoyama *et al*. (136)	2022	Japan	I-III	331	Surgery	2	OS	1.949	1.100-3.451	2013-2017
Xiao *et al*. (137)	2022	China	I-IV	106	Surgery	5	Surgical complications	0.15	0.06-0.55	2014-2019

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

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

Author (Ref)	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Liu *et al*. (138)	2017	China	II,III	507	Surgery	1.93	OS	1.755	1.204-2.559	2005-2012
Zhang *et al*. (112)	2020	China	I-IV	273	Surgery	1.258	OS	0.646	0.448-0.932	2010-2014

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

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

Author (Ref)	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95% CI	Research duration
Cheng *et al*. (139)	2020	China	I-III	607	Surgery	0.63	OS	0.545	0.372-0.799	2013-2019
Okugawa *et al*. (140)	2020	Japan	I-IV	551	Surgery	8350	OS	2.03	1.42-2.9	2001-2011
Aoyama *et al*. (141)	2022	Japan	I-III	480	Surgery	7000	OS	1.634	1.004-2.658	2013-2017

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

and the occurrence of adverse events of chemotherapy. Therefore, the PNI may have some clinical impact in patients with unresectable gastric cancer who receive chemotherapy. Further studies are needed to clarify this issue.

Controlling Nutritional Status in Gastric Cancer Treatment

The controlling nutritional status (CONUT) score was developed as an accessible nutritional screening tool for evaluating a patient's 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 gastric cancer was first reported in 2018. Twenty-six studies have evaluated the clinical impact of the PNI in gastric cancer. Table VI summarizes each study (125-137). Among 11 studies that evaluated the CONUT score as a prognostic factor, 10 evaluated patients with resectable gastric cancer and one evaluated those with unresectable gastric cancer. In both settings, a high CONUT score was associated with a poor prognosis. The HR of the CONUT score for OS was

1.553-3.707 in the resectable setting. The cut-off value of the CONUT score was reported to be 0-5. In addition, four studies evaluated the CONUT score as a predictive factor for postoperative surgical complications. These studies showed that a high CONUT score was associated with postoperative surgical complications.

The Albumin-to-Globulin Ratio and the Lymphocyte-to-C-Reactive Protein Ratio in Gastric Cancer Treatment

Recently, the clinical utilities of albumin and globulin as tumor prognostic markers have aroused great interest. The albumin-to-globulin ratio (AGR), which is calculated as AGR=albumin/(total protein−albumin) has been considered a possible effective combination of two 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 (112, 138) and Table VIII (139-141) showed the clinical impacts of the AGR and LCR in gastric cancer treatment. However, limited studies have shown its significance as a prognostic factor in gastric cancer treatment. Additional studies are needed to clarify the clinical impact of the AGR and LCR in gastric cancer treatment.

Future Prospects for Nutrition and Inflammation Assessment Tools for Gastric Cancer Treatment

Thus far, various nutrition and inflammation assessment tools have been applied in gastric cancer treatment. To utilize the nutrition and inflammation assessment tools in gastric cancer treatment, the following points should be clarified. Firstly, it is necessary to set the optimal cut-off value for each nutrition and inflammation assessment tool. 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 used for each tool. In addition, the timing of the application of these tools is also unclear. Previous studies assessed each tool at the preoperative, postoperative, and pretreatment of chemotherapy. It is necessary to establish the optimal timing for assessment by these tools. Secondly, the mechanisms through which nutrition and inflammation affect the prognosis of gastric cancer are unclear. Recently, the nutrition and inflammation status has been reported to affect postoperative surgical complications, the introduction of chemotherapy, and adverse events of chemotherapy. Previous studies demonstrated that postoperative surgical complications and the management of chemotherapy affect survival of patients with gastric cancer. However, the precise mechanism through which the nutritional and inflammatory status – as assessed by these tools – influences gastric cancer prognosis is unclear. Thirdly, it is unclear whether nutrition and inflammation assessment using these tools will become promising aids for defining treatment approaches targeting nutrition/inflammation in gastric cancer. Recent studies have focused on introducing perioperative oral nutritional treatment for patients with gastrointestinal cancer. The clinical relationship between changes in the nutritional and inflammatory status and perioperative oral nutritional treatment still needs 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- and long-term oncological outcomes in patients with gastric cancer. However, the optimal cut-off values for each tool have not been established and the mechanism through which these parameters influence prognosis is unclear. To optimize the nutrition and inflammation assessment tools for gastric cancer, it is necessary to clarify these points in further studies.

Conflicts of interest

None.

Authors' Contributions

TA and KH 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 YM were involved in drafting the article or revising it critically for important intellectual content. TA, and KH gave their final approval of the version to be published.

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