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Review

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

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Abstract. *Perioperative adjuvant treatment and complete resection is the standard treatment for resectable pancreatic cancer and systemic chemotherapy is standard treatment for unresectable pancreatic cancer. To improve the survival of patients with pancreatic cancer, it is necessary to identify promising biomarkers to optimize the treatment. The availability of biomarkers may allow patients to receive a more aggressive or less toxic treatment. Recent studies showed that the inflammatory and nutritional status perioperatively and/or during chemotherapy affect short and long-term oncological outcomes in pancreatic cancer. Introduction of inflammatory and nutritional status evaluation in pancreatic cancer treatment might improve the postoperative surgical complications or chemotherapy-induced adverse events. However, to introduce these various nutritional and inflammation assessment tools in daily clinical practice, it is necessary to understand the characteristics of each nutrition and inflammation assessment tool. This review summarizes the background, current status, and future perspectives of nutrition and inflammation assessment tools in pancreatic cancer treatment.*

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Pancreatic cancer is one of the leading cancers in the world. Every year 496,000 patients suffer, and 466,000 patients die due to pancreatic cancer (1, 2). Perioperative adjuvant treatment and complete resection is the standard treatment for resectable pancreatic cancer and systemic chemotherapy is standard treatment for unresectable pancreatic cancer (3, 4). Although the survival rate after treatment is gradually improving, 5-years survival rates of both resectable and unresectable pancreatic cancer is poor. To improve the survival of patients with pancreatic cancer, it is necessary to identify a valid biomarker to optimize treatment. Such biomarker can guide treatment and the patients can receive the more aggressive or less toxic treatment.

Recent studies showed that inflammatory and nutritional status perioperatively and/or during chemotherapy affect for short and long-term oncological outcomes in various malignancies (5, 6). In pancreatic cancer, the usefulness of several inflammation and nutritional status indices, such as Glasgow Prognostic Score, Prognostic Nutritional Index, and Controlling Nutritional Status, have been reported (7-10). Introduction of inflammatory and nutritional status evaluation in pancreatic cancer treatment might improve the postoperative surgical complications or chemotherapy-related adverse events. However, to introduce these nutritional and inflammation assessment tools in daily clinical practice, it is necessary to understand the characteristics of each nutrition and inflammation assessment tool.

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

Clinical Impact of Glasgow Prognostic Score (GPS) and Modified Glasgow Prognostic Score (mGPS) in Pancreatic Cancer Treatment

Glasgow Prognostic Score (GPS) and modified Glasgow Prognostic Score (mGPS) are calculated by the serum C-reactive protein level and serum albumin level. The GPS

is categorized as follows: score 2 cases have both elevated CRP (>10 mg/l) and low albumin (<35 g/l); score 1 cases have elevated CRP (>10 mg/l) or low albumin (<35 g/l); and score 0 cases have both normal CRP (≤10 mg/l) and normal albumin (≥35 g/l). There were 19 studies evaluating the clinical impacts of GPS/mGPS in pancreatic cancer (11-29). The first study was reported in 2011. Jamieson evaluated the prognostic value of mGPS in 135 pancreatic cancer patients who received pancreaticoduodenectomy. They found that elevated GPS showed a clear difference in median overall survival. Median overall survival was 26.7 months in the mGPS 0 group, 16.5 months in mGPS 1 group, and 13.1 months in mGPS 2 group. They also found that elevated mGPS was one of the significant independent risk factors for poor overall survival (HR=2.26, 95%CI=1.43-3.57, $p<0.001$). So far, 9 studies used GPS and 10 studies used mGPS. Hazard ratio of GPS/mGPS was 0.4 to 4.93 in patients who received chemotherapy or chemoradiation therapy and 1.723 to 3.642 in patients who received curative resection. Previous studies evaluated the clinical impact of GPS/mGPS on long-term oncological outcomes (Table I). Among these studies, high score of GPS/mGPS was associated with poor prognosis. Further studies are needed to evaluate ad clarify the clinical impact of GPS/mGPS on short-term oncological outcomes, such as occurrence of postoperative surgical complications and continuation of perioperative adjuvant treatment.

Clinical Impact of Neutrophil to Lymphocyte Ratio (NLR) in Pancreatic Cancer Treatment

Neutrophil to lymphocyte ratio (NLR) is calculated using the serum neutrophil and lymphocyte numbers. The first study of NLR in pancreatic cancer was reported in 2010. In resectable setting, Bhati evaluated the prognostic value of NLR in 84 patients with pancreatic cancer who received pancreaticoduodenectomy (30). They found that elevated NLR showed a clear difference in median overall survival. Median overall survival was 5.9 months in the group with NLR of more than 4.0, 17.0 months in the group with NLR of 3.0 to 4.0, and 13.7 months in the group with NLR of less than 3.0. They also found that elevated NLR was one of the significant independent risk factors for poor overall survival (HR=1.784, 95%CI=1.085-2.934, $p=0.023$). In metastatic setting, one study evaluated the prognostic value of NLR in 95 pancreatic cancer patients who received chemotherapy (31). They found that elevated NLR (cutoff value 5) clearly showed a clear difference in median overall survival. Median overall survival was 2.4 months in the high NLR group and 7.7 months in the low NLR group. They also demonstrated that elevated NLR was one of the significant independent risk factors for poor overall survival (HR=4.489, 95%CI=1.372-14.692, $p=0.013$). So far, 44 studies showed the significant prognostic value of NLR in pancreatic cancer (32-73) (Table II). Hazard ratio of NLR was 0.31 to 9.13 in patients who received chemotherapy or chemoradiation therapy and 1.581 to 5.35 in patients who received curative resection. Previous studies set the cutoff value of NLR at 1.7 to 14.1. Change of NLR during the perioperative or chemotherapy treatment period affects long-term oncological outcomes. Further studies are needed to clarify this issue.

Clinical Impact of Prognostic Nutritional Index (PNI) in Pancreatic Cancer Treatment

The prognostic nutritional index (PNI) is calculated using the serum albumin level and the number of serum lymphocytes. The first study of PNI in pancreatic cancer was reported in 2010. Kanda evaluated the prognostic value of preoperative PNI in 268 patients with pancreatic cancer who received pancreaticoduodenectomy (74). They found that decreased PNI (cutoff value 45) clearly showed a clear difference in median overall survival. Median overall survival was 9.0 months in the low PNI group and 15.7 months in high PNI group. They found that decreased PNI was one of the significant independent risk factors for poor overall survival (HR=2.06, 95%CI=1.46-2.91, $p<0.001$). In addition, they demonstrated that preoperative PNI status affects the occurrence of postoperative surgical complications (POC). Incidence of the POC was 45% in the low PNI group and 27.3% in high PNI group ($p=0.007$). PNI was one of the significant predictors of POC. So far, 15 studies examined the significant prognostic value of PNI in pancreatic cancer (75-90) (Table III). Hazard ratio of PNI was 0.627 to 3.53 in patients who received chemotherapy and 0.359 to 6.803 in patients who received curative resection. Previous studies set the cutoff value of PNI at 36 to 53. Interestingly, there were 2 studies evaluating the clinical effects of PNI on continuation of adjuvant chemotherapy and postoperative deep venous thrombosis (DVT). Yamada *et al*. clarified the risk factors of continuation of postoperative adjuvant chemotherapy in 121 pancreatic cancer patients. They found that PNI (at first visit) was significantly different between the adjuvant chemotherapy complete group and adjuvant chemotherapy incomplete group (46.8 *vs*. 44.3, $p=0.017$). Moreover, PNI (at first visit) was one of the significant risk factors for completion of adjuvant chemotherapy (OR=0.92, 95%CI=0.84-0.99, $p=0.041$). In addition, Iguchi *et al*. evaluated preoperative PNI as a predictor of development of DVT in 100 patients with pancreatic cancer. When comparing preoperative PNI between non-DVT and DVT-groups, there was a marginally significant difference. Mean PNI was 46.4 in the DVT group and 43.7 in non-DVT group (0.079). They found that decreased PNI (cutoff value at 44.3) was one of the significant independent risk factors for DVT (OR=31.3, 95%CI=2.0-486.4, $p=0.014$). These results need to be confirmed by other studies.

Table I. *Clinical impacts of Glasgow Prognostic Score (GPS) and modified Glasgow Prognostic Score (mGPS) in pancreatic cancer treatment.*

Author	Ref	Year	Country	Type of GPS	Tumor stage	Sample size	Treatment	Cut-off value	Endpoint	HR	95%CI	Research duration
Jamieson	11	2011	UK	mGPS	I-IV	135	Surgery	0,1,2	OS	2.26	1.45-3.57	2002-2009
Jamieson	12	2012	UK	mGPS	I-IV	173	Surgery	0,1,2	OS	1.77	1.19-2.62	1997-2009
Torre	13	2012	Italy	mGPS	I-IV	101	Surgery	0-1 *vs*. 2	OS	1.7745	1.1869-2.6532	2003-2009
Kurahara	14	2015	Japan	GPS	IV	96	Chemoradiation therapy	0-1 *vs*. 2	OS	4.673	1.802-12.11	2005-2014
Morinaga	15	2015	Japan	GPS	I-IV	40	Surgery	0 *vs*. 1-2	PFS	3.265	1.564-6.805	2006-2009
Yamada	16	2016	Japan	mGPS	I-IV	379	Surgery	0-1 *vs*. 2	OS	1.723	1.062-2.702	2002-2014
Numata	17	2016	Japan	GPS	I-II	67	Surgery	0 *vs*. 1-2	OS	1.946	1.033-3.691	2007-2014
Imaoka	18	2016	Japan	mGPS	I-IV	807	Mix	0 *vs*. 1-2	OS	1:1.772, 2: 2.033	1: 1.417-2.215, 2: 1.284-3.219	2001-2013
Iino	19	2017	Japan	mGPS	IV	47	Chemotherapy	0 *vs*. 1-2	OS	3.38	1.35-8.46	2010-2015
Fujiwara	20	2018	Japan	GPS	I-IV	188	Surgery	0 *vs*. 1-2	OS	1:2.053, 2: 3.642	1: 1.310-3.217, 2: 2.216-5.987	2000-2015
Matsumoto	21	2019	Japan	mGPS	IV	66	Chemotherapy	0 *vs*. 1-2	OS	4.93	1.96-12.5	2013-2014
Hwang	22	2019	Korea	mGPS	IV	203	Chemotherapy	0 *vs*. 1-2	OS	1.64	1.16-2.30	2016
Satoi	23	2020	Japan	GPS	IV	99	Chemotherapy	1-2 *vs*. 0	OS	0.4	0.21-0.76	2007-2014
Sawada	24	2020	Japan	GPS	IV	104	Chemotherapy	1-2 *vs*. 0	OS	0.47	0.29-0.76	2015-2019
Yamada	25	2021	Japan	mGPS	I, II	120	Surgery	0-1 *vs*. 2	CSS	2.36	1.08-5.10	2006-2019
Strijker	26	2021	Netherlands	GPS and mGPS	IV	4248	Mix	0 *vs*. 1-2	90-day mortality	GPS: 1.76-3.28, mGPS: 2.08-3.52	GPS: 1.11-5.36, mGPS: 1.34-5.61	2015-2017
Ushida	27	2021	Japan	mGPS	I-IV	431	Surgery	0-1 *vs*. 2	OS	1.73	1.07-2.81	2007-2014
Ohwada	28	2022	Japan	GPS	IV	96	Chemotherapy	0-1 *vs*. 2	OS	4.71	1.01-22.1	2014-2020
Kawakami	29	2023	Japan	GPS	IV	55	Chemotherapy	0 *vs*. 1-2	OS	2.46	1.15-5.25	2020-2021

Table II. *Clinical impacts of neutrophil to lymphocyte ratio (NLR) in pancreatic cancer treatment.*

Author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	HR	95%CI	Research duration
Bhatti	30	2010	UK		84	Surgery	4	OS	1.784	1.085-2.934	1998-2008
An	31	2010	China	IV	95	Chemotherapy	5	OS	4.489	1.372-14.692	2001-2008
Szkandera	32	2013	Austria	IV	474	Chemotherapy	2.3	CSS	1.24	1.01-1.51	2004-2012
Sugiura	33	2013	Japan	IV	83	Chemotherapy	4	OS	5.4	2.9-9.91	2002-2012
Xue	34	2014	Japan	IV	252	Chemotherapy	5	OS	1.58	1.08-2.31	2006-2012
Luo	35	2015	China	IV	403	Chemotherapy	3.1	OS	1.42	1.15-1.74	2002-2013
Goldstein	36	2015	Australia	IV	861	Chemotherapy	5	OS	0.57	0.48-0.68	2011-2013
Hasegawa	37	2016	Japan	I-IV	56	Surgery	2.2	OS	5.35	1.21-38.03	2007-2012
Suzuki	38	2016	Japan	IV	31	Chemotherapy	2.5	OS	0.41	0.19-0.90	2006-2014
Asaoka	39	2016	Japan	I-III	46	Surgery	2.7	OS	3.668	1.45-9.81	2007-2012
Lee	40	2016	Korea	IV	82	Chemotherapy	5	OS	2.76	1.33-5.75	2011-2014
Kobayashi	41	2016	Japan	II-IV	36	Chemotherapy	5	OS	9.13	2.03-41.06	2010-2014
Chen	42	2017	China	IV	132	Chemotherapy	2.78	OS	2.196	1.472-3.277	2010-2015
Sugiura	43	2017	Japan	IV	129	Palliative intervention	4	OS	4.01	2.54-6.34	2002-2015
Fang	44	2018	China	I-III	389	Surgery	2.2	OS	1.581	1.222-2.047	2008-2015
Abe	45	2018	Japan	I-IV	138	Surgery	2.2	OS	1.746	1.106-2.757	2004-2014
Kim	46	2018	Korea	I-III	62	Surgery	2.8	DFS	1.819	1.124-3.029	2005-2015
Song	47	2018	China	IV	59	Chemotherapy	3.75	OS	3.698	2.044-6.692	2010-2015
Giakoustidis	48	2018	UK	I-IV	127	Surgery	4	OS	2.05	1.11-3.78	2000-2014
Ventriglia	49	2018	Italy	IV	70	Chemotherapy	5	OS	2.7	1.4-5.2	2012-2015
Kubo	50	2019	Japan	I-IV	119	Surgery	3	OS	2.24	1.28-3.91	2009-2017
Rochefort	51	2019	France	IV	94	Chemotherapy	5	OS	0.31	0.11-0.84	2010-2015
Schlick	52	2019	Austria	III-IV	240	Chemotherapy	6	OS	1.7	1.2-2.6	2007-2016
Pu	53	2019	China	I-III	97	Surgery	14.1	OS	1.618	1.014-2.582	2012-2016
Cetin	54	2020	Turkey	IV	118	Chemotherapy	3.54	OS	2.17	1.17-4.03	2013-2017
Iwai	55	2020	Japan	IV	119	Chemotherapy	3.74	OS	2.43	1.484-3.977	2006-2018
Kim	56	2020	Korea	IV	302	Chemotherapy	3.8	OS	1.712	1.326-2.211	2004-2016
Shusterman	57	2020	USA	IV	226	Chemotherapy	5	OS	1.9	1.384-2.596	2006-2015
Pointer	58	2020	USA	Resectable to borderline resectable	277	Surgery	5	OS	2.13	1.41-3.22	2007-2015
Shin	59	2021	Korea	Locally advanced to borderline resectable	271	Chemotherapy	2.62	OS	2.47	1.84-3.32	2010-2017
Zhou	60	2021	China	Locally advanced to borderline resectable	241	Surgery	2.9	OS	3.138	2.234-4.410	2011-2019
Terao	61	2021	Japan	IV	153	Chemotherapy	4.5	OS	3.45	2.22-5.36	2011-2013
McLellan	62	2021	France	IV	212	Chemotherapy	5	OS	2.01	1.33-3.05	2010-2016
Frigerio	63	2022	Italy	IV	52	Surgery	1.7	OS	2.5	1.30-4.93	2008-2020
Ji	64	2022	China	IV	22	Radiation therapy	2.1	OS	4.05	1.21-13.59	2010-2020
Reddy	65	2022	US	Locally advanced to borderline resectable	156	Chemo radiation therapy	2.6	OS	2.55	1.20-5.45	2016-2018
Topkan	66	2022	Turkey	Locally advanced to borderline resectable	126	Chemo radiation therapy	3.1	OS	3.72	none	2007-2019
Reddy	67	2022	US	IV	68	Chemo radiation therapy	3.2	OS	1.14	1.04-1.23	2016-2021
Chen	68	2022	Taiwan	IV	57	Radiation therapy	3.5	OS	8.245	2.685-25.32	2009-2019
Marschner	69	2022	Germany	IV	1062	Chemotherapy	4	OS	1.57	1.34-1.83	2014-2020
Miki	70	2022	Japan	IV	40	Chemotherapy	4	OS	4.88	2.10-11.3	2020-2021
Mie	71	2023	Japan	IV	103	Chemotherapy	3	OS	0.51	0.32-0.80	2015-2022
Ma	72	2023	Canada	IV	263	Chemotherapy	5	OS	1.7	1.27-2.28	2015-2020
Maloney	73	2023	Australia	I-III	196	Surgery	5	OS	3.04	1.20-7.71	2014-2020

Table III. *Clinical impacts of prognostic nutritional index (PNI) in pancreatic cancer treatment.*

Author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	Hazard ratio	95%CI	Research duration
Kanda	74	2010	Japan	I-IV	268	Surgery	45	OS	1.73	1.21-2.47	1981-2009
Geng	75	2015	China	III, IV	211	Chemotherapy	47.3	OS	0.627	0.453-0.868	2011-2013
Ikeguchi	76	2017	Japan	I-III	43	Surgery	44.7	OS	6.803	1.919-24.39	2006-2015
Yamada	77	2017	Japan	I-III	117	Surgery	-	Complete adjuvant chemotherapy rate	0.92	0.84-0.99	2007-2013
Nakagawa	78	2018	Japan	I-IV	151	Surgery	40	DFS	0.37	0.43-0.95	2002-2014
Okabayashi	79	2018	Japan	I-III	240	Surgery	47.8	DSS	2.08	1.68-3.20	2005-2015
Nakagawa	80	2019	Japan	I-IV	263	Surgery	40	OS	2.019	1.348-3.239	2006-2015
Shimizu	81	2019	Japan	IV	93	Chemotherapy	43	OS	3.53	1.057-14.21	2008-2014
Iguchi	82	2020	Japan	-	100	Surgery	44.3	DVT	31.3	2.0-486.4	2015-2018
Kim	83	2020	Korea	I-IV	107	Surgery	Change of PNI -1.94	OS	3.516	1.8885-6.558	2003-2016
Onoe	84	2021	Japan	I-IV	187	Surgery	36	OS	1.6	1.11-2.30	2008-2018
Itoh	85	2021	Japan	I-III	589	Surgery	46	OS	1.432	1.069-1.918	2004-2016
Schlanger	86	2022	Romania	I-III	312	Surgery	40	OS	0.46	0.28-0.75	2012-2019
Igarashi	87	2022	Japan	IV	41	Conversion Surgery	41.7	OS	0.05	0.01-0.62	2014-2020
Jiang	88	2022	China	-	207	Surgery	45.1	OS	0.359	0.256-0.502	2018-2019
Frigerio	89	2022	Austria	Resectable-Locally advanced/ borderline resectable	52	Surgery	53	OS	2.6	1.23-5.30	2008-2020
Yang	90	2023	China	IV	44	Chemotherapy	43.7	OS	2.252	1.021-4.959	2017-2022

Clinical Impact of C-reactive Protein to Albumin Ratio (CAR) in Pancreatic Cancer Treatment

C-reactive protein to albumin ratio (CAR) is calculated using the levels of serum C-reactive protein and albumin. The first study of CAR in pancreatic cancer was reported in 2016. Wu evaluated the prognostic value of CAR in 386 patients with pancreatic cancer (91). According to receiver operating characteristics curves, they set the cutoff value of CAR at 0.180. They found that CAR high group (CAR ≥0.18) had significantly worse prognosis than the CAR low group (CAR <0.18). They found that high CAR was one of the significant independent risk factors for poor overall survival (HR=2.07, 95%CI=1.59-2.70, $p<0.001$). So far, 9 studies examined the prognostic value of PNI in pancreatic cancer (92-101) (Table IV). The HR of PNI was 1.45 to 4.00. Previous studies set the cutoff value of CAR at 0.03 to 3.85. There were 2 studies evaluating the impacts of CAR on the occurrence postoperative pancreatic fistula and pathological response. Funamizu *et al*. evaluated the clinical impact of CAR on postoperative pancreatic fistula (POPF) in 72 patients with pancreatic cancer who received distal pancreatomy. When comparing CAR between the POPF and non-POPF groups, there was a statistically significant difference in mean preoperative CAR (0.35 *vs*. 0.03, $p=0.001$). They demonstrated that high CAR (≥0.05) was one of the risk factors of POPE (OR=12.419, 95%CI=2.687-57.393, $p=0.013$). Moreover, Mori *et al*. evaluated the clinical impact of CAR on pathological response in 81 patients with pancreatic cancer who received neoadjuvant gemcitabine plus S-1 chemotherapy. They found that CAR >0.062 was independent predictor for Evans I disease (OR=5.310, 95%CI=1.354-20.829, $p=0.017$). They concluded that preoperative CAR was associated with poor pathological response.

Clinical Impact of Controlling Nutritional Status (CONUT) in Pancreatic Cancer Treatment

Controlling nutritional status (CONUT) is calculated using serum albumin and serum cholesterol levels, and total lymphocyte count. The nutritional status of patients with CONUT scores of 0-1, 2-4, 5-8, and 9-12 is normal, light, moderate, and severe, respectively. The higher the CONUT score, the worse the nutritional status. The first study of CONUT in pancreatic cancer was reported in 2018 (102). Kato *et al*. evaluated the prognostic value of CONUT in 344

Table IV. *Clinical impacts of C-reactive protein to albumin ratio (CAR) in pancreatic cancer treatment.*

Author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value of CAR	Endpoint	HR	95%CI	Research duration
Haruki	91	2016	Japan	0-IV	113	Surgery	0.03	OS	1.73	1.04-2.87	2001-2011
Wu	92	2016	China	III, IV	386	Mix	0.54	OS	4	2.64-6.03	2011-2014
Ikeguchi	93	2017	Japan	I-III	43	Surgery	0.04	OS	2.9	1.14-1.91	2006-2015
Hang	94	2017	China	III, IV	142	Chemotherapy	0.156	OS	1.629	1.097-2.419	2009-2014
Liu	95	2017	China	I-IV	386	Surgery	0.18	OS	2.07	1.59-2.70	2010-2015
Ikuta	96	2018	Japan	I-IV	136	Surgery	0.09	OS	1.978	1.051-3.724	2005-2017
Kim	97	2020	Korea	NR	302	Mix	3.85	OS	1.45	1.11-1.91	2004-2016
van Wijk	98	2020	Netherlands	I-IV	163	Surgery	0.2	OS	1.745	1.200-2.539	2013-2018
Mori	99	2021	Japan	I-III	81	Neoadjuvant chemotherapy and Surgery	0.062	Pathological response	5.31	1.354-20.829	2013-2019
Terao	100	2021	Japan	IV	43	Palliative care	1.3	OS	3.33	1.51-7.35	2011-2013
Funamizu	101	2022	Japan	I-III	72	Surgery	0.05	Postoperative pancreatic fistula	12.419	2.687-57.393	2009-2022

Table V. *Clinical impacts of Controlling Nutritional Status (CONUT) in pancreatic cancer treatment.*

Author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value	Endpoint	Hazard ratio	95%CI	Research duration
Kato	102	2018	Japan	I-IV	344	Surgery	4	OS	1.64	1.19-2.26	2002-2016
Wang	103	2020	China	I-III	294	Surgery	3	OS	4	2.82-5.67	2012-2019
Shiihara	104	2021	Japan	I-IV	206	Surgery	3	Postoperative complications (CD grade ≥IIIa)	5.89	1.01-34.5	2005-2016
Terasaki	105	2021	Japan	I-IV	307	Surgery and Chemotherapy	4	OS	1.75	1.01-3.05	2007-2015
Uemura	106	2022	Japan	IV	110	Chemotherapy	2	OS	1.92	1.16-3.24	2014-2020
Dang	107	2022	China	I-IV	384	Surgery	2	OS	1.145	1.051-1.248	2014-2018

patients with pancreatic cancer who received pancreatomy. They set the cutoff value of CONUT at 4. Median OS was 26.8 months in the CONUT low group (CONUT <4) and 18.0 months in the CONUT high group (CONUT ≥4); The difference was statistically significant. They clarified that high CONUT was one of the significant independent risk factors for poor overall survival (HR=1.64, 95%CI=1.19-2.26, p=0.003). So far, 6 studies examined the prognostic value of CONUT in pancreatic cancer (103-107) (Table V). Among them, 5 studies evaluated the clinical impact of CONUT on resectable cancer and one study on unresectable cancer. In the resectable setting, the HR of CONUT was 1.145 to 4 and the cutoff value 2 to 4. One study examined the association between CONUT and postoperative surgical complications (POC). Shiihara *et al*. evaluated the predictive value of CONUT for POC in 206 patients with pancreatic cancer who received pancreaticoduodenectomy. They reported that incidence of postoperative complications (Clavien–Dindo grade ≥IIIb) was significantly higher in the CONUT high group (CONUT ≥5) than in the CONUT low group (CONUT 0-4) (20.0% *vs*. 3.1%, p=0.020). They demonstrated that high CONUT was one of the risk factors of POC (OR=5.89, 95%CI=1.01-34.5, p=0.038).

Clinical Impact of Platelet to Lymphocyte Ratio (PLR) in Pancreatic Cancer Treatment

Platelet to lymphocyte ratio (PLR) is calculated using the platelet and total lymphocyte count. The first study of PLR in pancreatic cancer was reported in 2015. Shirai evaluated the prognostic value of PLR in 131 patients with pancreatic cancer who received pancreatomy (108). They set the cutoff

Table VI. *Clinical impacts of platelet to lymphocyte ratio (PLR) in pancreatic cancer treatment.*

Author	Ref	Year	Country	Tumor stage	Sample size	Therapy	Cut-off value of PLR	Endpoint	HR	95%CI	Research duration
Shirai	108	2015	Japan	-	131	Surgery	150	OS	1.688	1.045-2.726	2000-2013
Li	109	2018	USA	IV	134	Chemotherapy	123	OS	1.721	1.162-2.550	2010-2015
Hashimoto	110	2020	Japan	I-IV	229	Surgery	117	OS	3.137	1.335-7.367	1995-2016
Kim	111	2020	Korea	IV	302	Chemotherapy	180	OS	1.345	1.048-1.726	2004-2016
Schlanger	112	2022	Romania	I-III	312	Surgery	250	OS	1.6	1.2-2.1	2012-2019

value of PLR at 150. PLR status was a significant risk factor for both OS (HR=1.688, 95%CI=1.045-2.726, p=0.032) and RFS (HR=1.528, 95%CI=1.005-2.322, p=0.047). So far, 5 studies examined the significant prognostic value of PLR in pancreatic cancer (109-112) (Table VI); three for resectable and two for unresectable cancer. The HR of PLR was 1.345 to 3.137 and the cutoff value of PLR was 117 to 250. However, all studies examined the clinical impact on long-term oncological outcomes. Therefore, further studies are needed to evaluate the impact of PLR on short-term oncological outcomes, such as incidence of postoperative surgical complications, continuation of chemotherapy, and incidence of adverse events due to chemotherapy.

The Future Application of Tools for the Assessment of Nutrition and Inflammation in Pancreatic Cancer Treatment

Various studies have evaluated different nutrition and inflammation assessment tools in pancreatic cancer treatment. Before they can be applied in the clinical setting, further studies are needed to determine the optimal cutoff value of each tool as various cutoff values have been reported. These differences arise from heterogeneity in patient background factors as well as the methods of treatment and evaluation. In addition, the optimal timing for the application of each tool remains to be determined. In previous reports, assessments using each tool were applied at different time points, including the diagnosis, first visit, preoperatively, postoperatively, and before the initiation of chemotherapy. Thus, the optimal timing for the application of these tools should be determined. Finally, the underlying mechanisms through which nutrition and inflammation affect gastric cancer prognosis remain to be elucidated. The nutrition and inflammation status was recently reported to impact postoperative surgical complications, the introduction of chemotherapy, and adverse events of chemotherapy. Postoperative surgical complications and chemotherapy management have previously been reported to affect the survival of patients with pancreatic cancer. However, the precise mechanisms through which the nutritional and inflammatory status, as assessed by these tools, influence the prognosis of patients with pancreatic cancer remains unclear.

Conclusion

The nutritional and inflammatory status may have some clinical influence on both the short- and long-term oncological outcomes in patients with pancreatic cancer. However, the optimal cutoff values of each nutrition and inflammation assessment tool are unclear and the mechanism through which these parameters influence the prognosis is unclear. To optimize the nutrition and inflammation assessment tools for pancreatic cancer patients, it is necessary to clarify these points in further studies.

Conflicts of Interest

The Authors declare no conflicts of interest in association with the present study.

Authors' Contributions

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

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References

1 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68(6): 394-424, 2018. DOI: 10.3322/caac.21492

2 Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F: Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71(3): 209-249, 2021. DOI: 10.3322/caac.21660

3 Tempero MA, Malafa MP, Al-hawary M, Behrman SW, Benson AB, Cardin DB, Chiorean EG, Chung V, Czito B, Del Chiaro M, Dillhoff M, Donahue TR, Dotan E, Ferrone CR, Fountzilas C, Hardacre J, Hawkins WG, Klute K, Ko AH, Kunstman JW, Loconte N, Lowy AM, Moravek C, Nakakura EK, Narang AK, Obando J, Polanco PM, Reddy S, Reyngold M, Scaife C, Shen J, Vollmer C, Wolff RA, Wolpin BM, Lynn B, George GV: Pancreatic adenocarcinoma, Version 2.2021, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 19(4): 439-457, 2021. DOI: 10.6004/jnccn.2021.0017

4 Okusaka T, Furuse J: Recent advances in chemotherapy for pancreatic cancer: evidence from Japan and recommendations in guidelines. J Gastroenterol 55(4): 369-382, 2020. DOI: 10.1007/s00535-020-01666-y

5 Aoyama T, Hara K, Kazama K, Maezawa Y: Clinical impact of nutrition and inflammation assessment tools in gastric cancer treatment. Anticancer Res 42(11): 5167-5180, 2022. DOI: 10.21873/anticanres.16023

6 Aoyama T, Kazama K, Maezawa Y, Hara K: Usefulness of nutrition and inflammation assessment tools in esophageal cancer treatment. In Vivo 37(1): 22-35, 2023. DOI: 10.21873/invivo.13051

7 Li S, Tian G, Chen Z, Zhuang Y, Li G: Prognostic role of the prognostic nutritional index in pancreatic cancer: A meta-analysis. Nutr Cancer 71(2): 207-213, 2019. DOI: 10.1080/01635581.2018.1559930

8 Ma X, Zou W, Sun Y: Prognostic value of pretreatment controlling nutritional status score for patients with pancreatic cancer: A meta-analysis. Front Oncol 11: 770894, 2022. DOI: 10.3389/fonc.2021.770894

9 Riauka R, Ignatavicius P, Barauskas G: Preoperative platelet to lymphocyte ratio as a prognostic factor for resectable pancreatic cancer: A systematic review and meta-analysis. Dig Surg 37(6): 447-455, 2020. DOI: 10.1159/000508444

10 Zhou Y, Wei Q, Fan J, Cheng S, Ding W, Hua Z: Prognostic role of the neutrophil-to-lymphocyte ratio in pancreatic cancer: A meta-analysis containing 8252 patients. Clin Chim Acta 479: 181-189, 2018. DOI: 10.1016/j.cca.2018.01.024

11 Jamieson NB, Denley SM, Logue J, Mackenzie DJ, Foulis AK, Dickson EJ, Imrie CW, Carter R, Mckay CJ, Mcmillan DC: A prospective comparison of the prognostic value of tumor- and patient-related factors in patients undergoing potentially curative surgery for pancreatic ductal adenocarcinoma. Ann Surg Oncol 18(8): 2318-2328, 2011. DOI: 10.1245/s10434-011-1560-3

12 Jamieson NB, Mohamed M, Oien KA, Foulis AK, Dickson EJ, Imrie CW, Carter CR, Mckay CJ, Mcmillan DC: The relationship between tumor inflammatory cell infiltrate and outcome in patients with pancreatic ductal adenocarcinoma. Ann Surg Oncol 19(11): 3581-3590, 2012. DOI: 10.1245/s10434-012-2370-y

13 La Torre M, Nigri G, Cavallini M, Mercantini P, Ziparo V, Ramacciato G: The glasgow prognostic score as a predictor of survival in patients with potentially resectable pancreatic adenocarcinoma. Ann Surg Oncol 19(9): 2917-2923, 2012. DOI: 10.1245/s10434-012-2348-9

14 Kurahara H, Maemura K, Mataki Y, Sakoda M, Iino S, Hiwatashi K, Kawasaki Y, Arigami T, Ishigami S, Kijima Y, Shinchi H, Takao S, Natsugoe S: Prognostication by inflammation-based score in patients with locally advanced pancreatic cancer treated with chemoradiotherapy. Pancreatology 15(6): 688-693, 2015. DOI: 10.1016/j.pan.2015.09.015

15 Morinaga S, Murakawa M, Katayama Y, Yamaoku K, Aoyama T, Kanazawa A, Higuchi A, Shiozawa M, Kobayashi S, Ueno M, Morimoto M: Glasgow prognostic score predicts clinical outcomes in patients with pancreatic cancer undergoing adjuvant gemcitabine monotherapy after curative surgery. Anticancer Res 35: 4865-4870, 2015.

16 Yamada S, Fujii T, Yabusaki N, Murotani K, Iwata N, Kanda M, Tanaka C, Nakayama G, Sugimoto H, Koike M, Fujiwara M, Kodera Y: clinical implication of inflammation-based prognostic score in pancreatic cancer: Glasgow prognostic score is the most reliable parameter. Medicine (Baltimore) 95(18): e3582, 2016. DOI: 10.1097/MD.0000000000003582

17 Numata K, Morinaga S, Katayama Y, Sawazaki S, Numata M, Godai T, Higuchi A, Shiozawa M, Rino Y, Masuda M, Akaike M: Combining the Glasgow Prognostic Score and serum carbohydrate antigen 19-9 level improves the ability to predict early recurrence in resected pancreatic cancer patients receiving adjuvant gemcitabine. Anticancer Res 36: 2467-2474, 2016.

18 Imaoka H, Mizuno N, Hara K, Hijioka S, Tajika M, Tanaka T, Ishihara M, Yogi T, Tsutsumi H, Fujiyoshi T, Sato T, Shimizu Y, Niwa Y, Yamao K: Evaluation of modified glasgow prognostic score for pancreatic cancer. Pancreas 45(2): 211-217, 2016. DOI: 10.1097/MPA.0000000000000446

19 Iino C, Shimoyama T, Igarashi T, Aihara T, Ishii K, Sakamoto J, Tono H, Fukuda S: Biliary drainage improves the predictive value of modified Glasgow Prognostic Scores in inoperable pancreatic cancer. PLoS One 12(6): e0178777, 2017. DOI: 10.1371/journal.pone.0178777

20 Fujiwara Y, Haruki K, Shiba H, Hamura R, Horiuchi T, Shirai Y, Furukawa K, Gocho T, Yanaga K: C-Reactive protein-based prognostic measures are superior at predicting survival compared with peripheral blood cell count-based ones in patients after curative resection for pancreatic cancer. Anticancer Res 38(11): 6491-6499, 2018. DOI: 10.21873/anticanres.13013

21 Matsumoto I, Kamei K, Omae K, Suzuki S, Matsuoka H, Mizuno N, Ozaka M, Ueno H, Kobayashi S, Uesugi K, Kobayashi M, Todaka A, Fukutomi A: FOLFIRINOX for locally advanced pancreatic cancer: Results and prognostic factors of subset analysis from a nation-wide multicenter observational study in Japan. Pancreatology 19(2): 296-301, 2019. DOI: 10.1016/j.pan.2019.01.001

22 Hwang I, Kang J, Ip HNN, Jeong JH, Kim K, Chang H, Yoo C, Ryoo B: Prognostic factors in patients with metastatic or recurrent pancreatic cancer treated with first-line nab-paclitaxel plus gemcitabine: implication of inflammation-based scores. Invest New Drugs 37(3): 584-590, 2019. DOI: 10.1007/s10637-018-0681-y

23 Satoi S, Yamamoto T, Uchida K, Fujii T, Kin T, Hirano S, Hanada K, Itoi T, Murakami Y, Igarashi H, Eguchi H, Kuroki T, Shimizu Y, Tani M, Tanno S, Tsuji Y, Hirooka Y, Masamune A, Shimokawa T, Yamaue H, Okazaki K: Optimal treatment for octogenarians with resectable and borderline resectable pancreatic ductal adenocarcinoma. Pancreas 49(6): 837-844, 2020. DOI: 10.1097/MPA.0000000000001579

24 Sawada M, Kasuga A, Mie T, Furukawa T, Taniguchi T, Fukuda K, Yamada Y, Takeda T, Kanata R, Matsuyama M, Sasaki T,

Ozaka M, Sasahira N: Modified FOLFIRINOX as a second-line therapy following gemcitabine plus nab-paclitaxel therapy in metastatic pancreatic cancer. BMC Cancer 20(1): 449, 2020. DOI: 10.1186/s12885-020-06945-8

25 Yamada S, Shimada M, Morine Y, Imura S, Ikemoto T, Saito Y, Miyazaki K, Tokunaga T, Nishi M: Significance of frailty in prognosis after surgery in patients with pancreatic ductal adenocarcinoma. World J Surg Oncol 19(1): 94, 2021. DOI: 10.1186/s12957-021-02205-6

26 Strijker M, van Veldhuisen E, van der Geest LG, Busch OR, Bijlsma MF, Haj Mohammad N, Homs MY, van Hooft JE, Verheij J, de Vos-Geelen J, Wilmink JW, Steyerberg WEW, Besselink MG, van Laarhoven HW, Dutch Pancreatic Cancer Group: Readily available biomarkers predict poor survival in metastatic pancreatic cancer. Biomarkers 26: 325-334, 2021. DOI: 10.1080/1354750X.2021.1893814

27 Ushida Y, Inoue Y, Ito H, Oba A, Mise Y, Ono Y, Sato T, Saiura A, Takahashi Y: High CA19-9 level in resectable pancreatic cancer is a potential indication of neoadjuvant treatment. Pancreatology 21(1): 130-137, 2021. DOI: 10.1016/j.pan.2020.11.026

28 Ohwada S, Todaka A, Nakase H, Shirasu H, Kawakami T, Hamauchi S, Tsushima T, Yokota T, Onozawa Y, Yasui H, Yamazaki K: Effectiveness and safety of gemcitabine plus nab-paclitaxel in elderly patients with advanced pancreatic cancer: a single-center retrospective cohort study. Invest New Drugs 40(5): 1106-1116, 2022. DOI: 10.1007/s10637-022-01221-x

29 Kawakami T, Todaka A, Oshima K, Fushiki K, Hamauchi S, Tsushima T, Yokota T, Onozawa Y, Yasui H, Yamazaki K: Biomarker analysis for patients with pancreatic cancer treated with nanoliposomal irinotecan plus 5-fluorouracil/leucovorin. BMC Cancer 23(1): 68, 2023. DOI: 10.1186/s12885-023-10542-w

30 Bhatti I, Peacock O, Lloyd G, Larvin M, Hall RI: Preoperative hematologic markers as independent predictors of prognosis in resected pancreatic ductal adenocarcinoma: neutrophil-lymphocyte versus platelet-lymphocyte ratio. Am J Surg 200(2): 197-203, 2010. DOI: 10.1016/j.amjsurg.2009.08.041

31 An X, Ding P, Li Y, Wang F, Shi Y, Wang Z, He Y, Xu R, Jiang W: Elevated neutrophil to lymphocyte ratio predicts survival in advanced pancreatic cancer. Biomarkers 15(6): 516-522, 2010. DOI: 10.3109/1354750X.2010.491557

32 Szkandera J, Stotz M, Eisner F, Absenger G, Stojakovic T, Samonigg H, Kornprat P, Schaberl-Moser R, Alzoughbi W, Ress AL, Seggewies FS, Gerger A, Hoefler G, Pichler M: External validation of the derived neutrophil to lymphocyte ratio as a prognostic marker on a large cohort of pancreatic cancer patients. PLoS One 8(11): e78225, 2013. DOI: 10.1371/journal.pone.0078225

33 Sugiura T, Uesaka K, Kanemoto H, Mizuno T, Okamura Y: Elevated preoperative neutrophil-to-lymphocyte ratio as a predictor of survival after gastroenterostomy in patients with advanced pancreatic adenocarcinoma. Ann Surg Oncol 20(13): 4330-4337, 2013. DOI: 10.1245/s10434-013-3227-8

34 Xue P, Kanai M, Mori Y, Nishimura T, Uza N, Kodama Y, Kawaguchi Y, Takaori K, Matsumoto S, Uemoto S, Chiba T: Neutrophil-to-lymphocyte ratio for predicting palliative chemotherapy outcomes in advanced pancreatic cancer patients. Cancer Med 3(2): 406-415, 2014. DOI: 10.1002/cam4.204

35 Luo G, Guo M, Liu Z, Xiao Z, Jin K, Long J, Liu L, Liu C, Xu J, Ni Q, Yu X: Blood Neutrophil–lymphocyte ratio predicts survival in patients with advanced pancreatic cancer treated with chemotherapy. Ann Surg Oncol 22(2): 670-676, 2015. DOI: 10.1245/s10434-014-4021-y

36 Goldstein D, El-maraghi RH, Hammel P, Heinemann V, Kunzmann V, Sastre J, Scheithauer W, Siena S, Tabernero J, Teixeira L, Tortora G, Van Laethem J, Young R, Penenberg DN, Lu B, Romano A, Von Hoff DD: Nab-paclitaxel plus gemcitabine for metastatic pancreatic cancer: Long-term survival from a phase III trial. J Natl Cancer Inst 107(2): dju413-dju413, 2015. DOI: 10.1093/jnci/dju413

37 Hasegawa S, Eguchi H, Tomokuni A, Tomimaru Y, Asaoka T, Wada H, Hama N, Kawamoto K, Kobayashi S, Marubashi S, Konnno M, Ishii H, Mori M, Doki Y, Nagano H: Pre-treatment neutrophil to lymphocyte ratio as a predictive marker for pathological response to preoperative chemoradiotherapy in pancreatic cancer. Oncol Lett 11(2): 1560-1566, 2016. DOI: 10.3892/ol.2015.4057

38 Suzuki R, Takagi T, Hikichi T, Konno N, Sugimoto M, Watanabe K, Nakamura J, Waragai Y, Kikuchi H, Takasumi M, Watanabe H, Ohira H: Derived neutrophil/lymphocyte ratio predicts gemcitabine therapy outcome in unresectable pancreatic cancer. Oncol Lett 11(5): 3441-3445, 2016. DOI: 10.3892/ol.2016.4381

39 Asaoka T, Miyamoto A, Maeda S, Tsujie M, Hama N, Yamamoto K, Miyake M, Haraguchi N, Nishikawa K, Hirao M, Ikeda M, Sekimoto M, Nakamori S: Prognostic impact of preoperative NLR and CA19-9 in pancreatic cancer. Pancreatology 16(3): 434-440, 2016. DOI: 10.1016/j.pan.2015.10.006

40 Lee JM, Lee HS, Hyun JJ, Choi HS, Kim ES, Keum B, Seo YS, Jeen YT, Chun HJ, Um SH, Kim CD: Prognostic value of inflammation-based markers in patients with pancreatic cancer administered gemcitabine and erlotinib. World J Gastrointest Oncol 8(7): 555-562, 2016. DOI: 10.4251/wjgo.v8.i7.555

41 Kobayashi S, Ueno M, Kameda R, Moriya S, Irie K, Goda Y, Tezuka S, Yanagida N, Ohkawa S, Aoyama T, Morinaga S, Morimoto M: Duodenal stenting followed by systemic chemotherapy for patients with pancreatic cancer and gastric outlet obstruction. Pancreatology 16(6): 1085-1091, 2016. DOI: 10.1016/j.pan.2016.07.007

42 Chen Y, Yan H, Wang Y, Shi Y, Dai G: Significance of baseline and change in neutrophil-to-lymphocyte ratio in predicting prognosis: a retrospective analysis in advanced pancreatic ductal adenocarcinoma. Sci Rep 7(1): 753, 2017. DOI: 10.1038/s41598-017-00859-5

43 Sugiura T, Okamura Y, Ito T, Yamamoto Y, Ashida R, Yoshida Y, Tanaka M, Uesaka K: Prognostic scoring system for patients who present with a gastric outlet obstruction caused by advanced pancreatic adenocarcinoma. World J Surg 41(10): 2619-2624, 2017. DOI: 10.1007/s00268-017-4027-2

44 Fang L, Xu X, Ji Y, Huang P: The prognostic value of preoperative neutrophil-to-lymphocyte ratio in resected patients with pancreatic adenocarcinoma. World J Surg 42(11): 3736-3745, 2018. DOI: 10.1007/s00268-018-4686-7

45 Abe T, Amano H, Kobayashi T, Hanada K, Nakahara M, Ohdan H, Noriyuki T: Preoperative neutrophil-to-lymphocyte ratio as a prognosticator in early stage pancreatic ductal adenocarcinoma. Eur J Surg Oncol 44(10): 1573-1579, 2018. DOI: 10.1016/j.ejso.2018.04.022

46 Kim W, Lim T, Park P, Choi S, Kim W: Prognostic impact of the combination of the neutrophil-to-lymphocyte ratio and serum carbohydrate antigen 19-9 in patients with pancreas head cancer. ANZ J Surg 89(7-8), 2019. DOI: 10.1111/ans.15029

47 Song J, Chen M, Guo J, Lian S, Xu B: Combined pretreatment serum CA19-9 and neutrophil-to-lymphocyte ratio as a potential prognostic factor in metastatic pancreatic cancer patients. Medicine (Baltimore) 97(4): e9707, 2018. DOI: 10.1097/MD.0000000000009707

48 Giakoustidis A, Neofytou K, Costa Neves M, Giakoustidis D, Louri E, Cunningham D, Mudan S: Identifying the role of neutrophil-to-lymphocyte ratio and platelets-to-lymphocyte ratio as prognostic markers in patients undergoing resection of pancreatic ductal adenocarcinoma. Ann Hepatobiliary Pancreat Surg 22(3): 197-207, 2018. DOI: 10.14701/ahbps.2018.22.3.197

49 Ventriglia J, Petrillo A, Huerta Alváro M, Laterza MM, Savastano B, Gambardella V, Tirino G, Pompella L, Diana A, Iovino F, Troiani T, Martinelli E, Morgillo F, Orditura M, Cervantes A, Ciardiello F, De Vita F: Neutrophil to lymphocyte ratio as a predictor of poor prognosis in metastatic pancreatic cancer patients treated with nab-paclitaxel plus gemcitabine: a propensity score analysis. Gastroenterol Res Pract 2018: 2373868, 2018. DOI: 10.1155/2018/2373868

50 Kubo H, Murakami T, Matsuyama R, Yabushita Y, Tsuchiya N, Sawada Y, Homma Y, Kumamoto T, Endo I: Prognostic impact of the neutrophil-to-lymphocyte ratio in borderline resectable pancreatic ductal adenocarcinoma treated with neoadjuvant chemoradiotherapy followed by surgical resection. World J Surg 43(12): 3153-3160, 2019. DOI: 10.1007/s00268-019-05159-9

51 Rochefort P, Lardy-Cleaud A, Sarabi M, Desseigne F, Cattey-Javouhey A, de la Fouchardière C: Long-term survivors in metastatic pancreatic ductal adenocarcinoma: A retrospective and matched pair analysis. Oncologist 24(12): 1543-1548, 2019. DOI: 10.1634/theoncologist.2018-0786

52 Schlick K, Magnes T, Huemer F, Ratzinger L, Weiss L, Pichler M, Melchardt T, Greil R and Egle A: C-reactive protein and neutrophil/lymphocytes ratio: Prognostic indicator for doubling overall survival prediction in pancreatic cancer patients. J Clin Med 8(11): 1791, 2019. DOI: 10.3390/jcm8111791

53 Pu N, Yin H, Zhao G, Nuerxiati A, Wang D, Xu X, Kuang T, Jin D, Lou W, Wu W: Independent effect of postoperative neutrophil-to-lymphocyte ratio on the survival of pancreatic ductal adenocarcinoma with open distal pancreatosplenectomy and its nomogram-based prediction. J Cancer 10(24): 5935-5943, 2019. DOI: 10.7150/jca.35856

54 Cetin S, Dede I: Prognostic value of the neutrophil-to-lymphocyte ratio and carbohydrate antigen 19-9 in estimating survival in patients with metastatic pancreatic cancer. J Cancer Res Ther 16(4): 909, 2020. DOI: 10.4103/jcrt.JCRT_366_19

55 Iwai N, Okuda T, Sakagami J, Harada T, Ohara T, Taniguchi M, Sakai H, Oka K, Hara T, Tsuji T, Komaki T, Kagawa K, Yasuda H, Naito Y, Itoh Y: Neutrophil to lymphocyte ratio predicts prognosis in unresectable pancreatic cancer. Sci Rep 10(1): 18758, 2020. DOI: 10.1038/s41598-020-75745-8

56 Kim HJ, Lee SY, Kim DS, Kang EJ, Kim JS, Choi YJ, Oh SC, Seo JH, Kim JS: Inflammatory markers as prognostic indicators in pancreatic cancer patients who underwent gemcitabine-based palliative chemotherapy. Korean J Intern Med 35(1): 171-184, 2020. DOI: 10.3904/kjim.2018.076

57 Shusterman M, Jou E, Kaubisch A, Chuy JW, Rajdev L, Aparo S, Tang J, Ohri N, Negassa A, Goel S: The neutrophil-to-lymphocyte ratio is a prognostic biomarker in an ethnically diverse patient population with advanced pancreatic cancer. J Gastrointest Cancer 51(3): 868-876, 2020. DOI: 10.1007/s12029-019-00316-8

58 Pointer DT Jr, Roife D, Powers BD, Murimwa G, Elessawy S, Thompson ZJ, Schell MJ, Hodul PJ, Pimiento JM, Fleming JB, Malafa MP: Neutrophil to lymphocyte ratio, not platelet to lymphocyte or lymphocyte to monocyte ratio, is predictive of patient survival after resection of early-stage pancreatic ductal adenocarcinoma. BMC Cancer 20(1): 750, 2020. DOI: 10.1186/s12885-020-07182-9

59 Shin K, Jung EK, Park SJ, Jeong S, Kim IH, Lee MA: Neutrophil-to-lymphocyte ratio and carbohydrate antigen 19-9 as prognostic markers for advanced pancreatic cancer patients receiving first-line chemotherapy. World J Gastrointest Oncol 13(8): 915-928, 2021. DOI: 10.4251/wjgo.v13.i8.915

60 Zhou L, Wang J, Zhang XX, Lyu SC, Pan LC, Du GS, Lang R, He Q: Prognostic value of preoperative nlr and vascular reconstructive technology in patients with pancreatic cancer of portal system invasion: A real world study. Front Oncol 11: 682928, 2021. DOI: 10.3389/fonc.2021.682928

61 Terao T, Kumagi T, Hyodo I, Yokota T, Azemoto N, Miyata H, Kuroda T, Ohno Y, Tanaka Y, Shibata N, Imamura Y, Kanemitsu K, Miyake T, Koizumi M, Hiasa Y, Ehime Pancreato-Cholangiology (EPOCH) Study Group: Simple prognostic markers for optimal treatment of patients with unresectable pancreatic cancer. Medicine (Baltimore) 100(43): e27591, 2021. DOI: 10.1097/MD.0000000000027591

62 Mclellan P, Henriques J, Ksontini F, Doat S, Hammel P, Desrame J, Trouilloud I, Louvet C, Pietrasz D, Vernerey D, Bachet J: Prognostic value of the early change in neutrophil-to-lymphocyte ratio in metastatic pancreatic adenocarcinoma. Clin Res Hepatol Gastroenterol 45(3): 101541, 2021. DOI: 10.1016/j.clinre.2020.08.016

63 Frigerio I, Malleo G, de Pastena M, Deiro G, Surci N, Scopelliti F, Esposito A, Regi P, Giardino A, Allegrini V, Bassi C, Girelli R, Salvia R, Butturini G: Prognostic factors after pancreatectomy for pancreatic cancer initially metastatic to the liver. Ann Surg Oncol 29(13): 8503-8510, 2022. DOI: 10.1245/s10434-022-12385-4

64 Ji X, Zhou B, Ding W, Wang J, Jiang W, Li Y, Hu J, Sun X: Efficacy of stereotactic body radiation therapy for locoregional recurrent pancreatic cancer after radical resection. Front Oncol 12: , 2022. DOI: 10.3389/fonc.2022.925043

65 Reddy AV, Hill CS, Sehgal S, He J, Zheng L, Herman JM, Meyer J, Narang AK: High neutrophil-to-lymphocyte ratio following stereotactic body radiation therapy is associated with poor clinical outcomes in patients with borderline resectable and locally advanced pancreatic cancer. J Gastrointest Oncol 13(1): 368-379, 2022. DOI: 10.21037/jgo-21-513

66 Topkan E, Selek U, Haksoyler V, Kucuk A, Durankus NK, Sezen D, Bolukbasi Y, Pehlivan B: Postchemoradiotherapy neutrophil-to-lymphocyte ratio predicts distant metastasis and survival results in locally advanced pancreatic cancers. Int J Clin Pract 2022: 7473649, 2022. DOI: 10.1155/2022/7473649

67 Reddy AV, Hill CS, Sehgal S, Zheng L, He J, Laheru DA, Jesus-Acosta A, Herman JM, Meyer J, Narang AK: Post-radiation neutrophil-to-lymphocyte ratio is a prognostic marker in patients with localized pancreatic adenocarcinoma treated with anti-PD-1 antibody and stereotactic body radiation therapy. Radiat Oncol J 40(2): 111-119, 2022. DOI: 10.3857/roj.2021.01060

68 Chen YL, Tsai CL, Cheng JC, Wang CW, Yang SH, Tien YW, Kuo SH: Competing risk analysis of outcomes of unresectable pancreatic cancer patients undergoing definitive radiotherapy. Front Oncol 11: 730646, 2022. DOI: 10.3389/fonc.2021.730646

69 Marschner N, Hegewisch-Becker S, Reiser M, von der Heyde E, Bertram M, Hollerbach SH, Kreher S, Wolf T, Binninger A, Chiabudini M, Kaiser-Osterhues A, Jänicke M, TPK-Group (Tumour Registry Pancreatic Cancer): FOLFIRINOX or gemcitabine/nab-paclitaxel in advanced pancreatic adenocarcinoma: A novel validated prognostic score to facilitate treatment decision-making in real-world. Int J Cancer 152(3): 458-469, 2023. DOI: 10.1002/ijc.34271

70 Miki M, Fujimori N, Ueda K, Lee L, Murakami M, Takamatsu Y, Shimokawa Y, Niina Y, Oono T, Hisano T, Furukawa M, Ogawa Y: Treatment effect and safety of nanoliposomal irinotecan with fluorouracil and folinic acid after gemcitabine-based therapy in patients with advanced pancreatic cancer: A multicenter, prospective observational study. J Clin Med 11(17): 2022. DOI: 10.3390/jcm11175084

71 Mie T, Sasaki T, Takeda T, Okamoto T, Hamada T, Ishitsuka T, Yamada M, Nakagawa H, Furukawa T, Kasuga A, Matsuyama M, Ozaka M, Sasahira N: Treatment outcomes and prognostic factors of gemcitabine plus nab-paclitaxel as second-line chemotherapy after modified FOLFIRINOX in unresectable pancreatic cancer. Cancers (Basel) 15(2): 358, 2023. DOI: 10.3390/cancers15020358

72 Ma LX, Wang Y, Espin-Garcia O, Allen MJ, Jang GH, Zhang A, Dodd A, Ramotar S, Hutchinson S, Tehfe M, Ramjeesingh R, Biagi J, Wilson JM, Notta F, Fischer SE, Zogopoulos G, Gallinger S, Grant RC, Khokha R, Chan N, Grünwald BT, Knox JJ, O'Kane GM: Systemic inflammatory prognostic scores in advanced pancreatic adenocarcinoma. Br J Cancer 128(10): 1916-1921, 2023. DOI: 10.1038/s41416-023-02214-0

73 Maloney S, Pavlakis N, Itchins M, Arena J, Mittal A, Hudson A, Colvin E, Sahni S, Diakos C, Chan D, Gill AJ, Samra J, Clarke SJ: The prognostic and predictive role of the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) as biomarkers in resected pancreatic cancer. J Clin Med 12(5): 1989, 2023. DOI: 10.3390/jcm12051989

74 Kanda M, Fujii T, Kodera Y, Nagai S, Takeda S, Nakao A: Nutritional predictors of postoperative outcome in pancreatic cancer. Br J Surg 98(2): 268-274, 2010. DOI: 10.1002/bjs.7305

75 Geng Y, Qi Q, Sun M, Chen H, Wang P, Chen Z: Prognostic nutritional index predicts survival and correlates with systemic inflammatory response in advanced pancreatic cancer. Eur J Surg Oncol 41(11): 1508-1514, 2015. DOI: 10.1016/j.ejso.2015.07.022

76 Ikeguchi M, Hanaki T, Endo K, Suzuki K, Nakamura S, Sawata T, Shimizu T: C-reactive protein/albumin ratio and prognostic nutritional index are strong prognostic indicators of survival in resected pancreatic ductal adenocarcinoma. J Pancreat Cancer 3(1): 31-36, 2017. DOI: 10.1089/pancan.2017.0006

77 Yamada D, Eguchi H, Asaoka T, Tomihara H, Noda T, Wada H, Kawamoto K, Gotoh K, Takeda Y, Tanemura M, Mori M, Doki Y: The basal nutritional state of PDAC patients is the dominant factor for completing adjuvant chemotherapy. Surg Today 47(11): 1361-1371, 2017. DOI: 10.1007/s00595-017-1522-x

78 Nakagawa S, Yamashita Y, Umezaki N, Yamao T, Okabe H, Imai K, Nitta H, Hashimoto D, Chikamoto A, Baba H: Serum marker score based on prognostic nutrition index, carcinoembryonic antigen, and carbohydrate antigen 19-9 is associated with recurrence for patients undergoing surgery for pancreatic ductal adenocarcinoma. Pancreas 47(9): 1130-1134, 2018. DOI: 10.1097/MPA.0000000000001146

79 Okabayashi T, Shima Y, Sumiyoshi T, Sui K, Iwata J, Morita S, Shimada Y, Iiyama T: A novel physiobiological parameter-based grading system for resectable pancreatic cancer. Ann Surg Oncol 25(7): 1889-1895, 2018. DOI: 10.1245/s10434-018-6485-7

80 Nakagawa K, Sho M, Akahori T, Nagai M, Nakamura K, Takagi T, Tanaka T, Nishiofuku H, Ohbayashi C, Kichikawa K, Ikeda N: Significance of the inflammation-based prognostic score in recurrent pancreatic cancer. Pancreatology 19(5): 722-728, 2019. DOI: 10.1016/j.pan.2019.05.461

81 Shimizu T, Taniguchi K, Asakuma M, Tomioka A, Inoue Y, Komeda K, Hirokawa F, Uchiyama K: Lymphocyte–to–monocyte ratio and prognostic nutritional index predict poor prognosis in patients on chemotherapy for unresectable pancreatic cancer. Anticancer Res 39(4): 2169-2176, 2019. DOI: 10.21873/anticanres.13331

82 Iguchi T, Sugimachi K, Mano Y, Kono M, Kagawa M, Nakanoko T, Uehara H, Sugiyama M, Ota M, Ikebe M, Morita M, Toh Y: The preoperative prognostic nutritional index predicts the development of deep venous thrombosis after pancreatic surgery. Anticancer Res 40(4): 2297-2301, 2020. DOI: 10.21873/anticanres.14195

83 Kim KH, Hwang HK, Kang IC, Lee WJ, Kang CM: Oncologic impact of preoperative prognostic nutritional index change in resected pancreatic cancer following neoadjuvant chemotherapy. Pancreatology 20(2): 247-253, 2020. DOI: 10.1016/j.pan.2019.12.006

84 Onoe S, Yokoyama Y, Kokuryo T, Igami T, Mizuno T, Yamaguchi J, Watanabe N, Kawakatsu S, Ebata T: A presurgical prognostic stratification based on nutritional assessment and carbohydrate antigen 19-9 in pancreatic carcinoma: An approach with nonanatomic biomarkers. Surgery 169(6): 1463-1470, 2021. DOI: 10.1016/j.surg.2020.11.035

85 Itoh S, Tsujita E, Fukuzawa K, Sugimachi K, Iguchi T, Ninomiya M, Maeda T, Kajiyama K, Adachi E, Uchiyama H, Utsunomiya T, Ikeda Y, Maekawa S, Toshima T, Harada N, Yoshizumi T, Mori M: Prognostic significance of preoperative PNI and CA19-9 for pancreatic ductal adenocarcinoma: A multi-institutional retrospective study. Pancreatology 21(7): 1356-1363, 2021. DOI: 10.1016/j.pan.2021.08.003

86 Schlanger D, Popa C, Paşca S, Seicean A, Al Hajjar N: The role of systemic immuno-inflammatory factors in resectable pancreatic adenocarcinoma: a cohort retrospective study. World J Surg Oncol 20(1): 144, 2022. DOI: 10.1186/s12957-022-02606-1

87 Igarashi T, Yamada S, Hoshino Y, Murotani K, Baba H, Takami H, Yoshioka I, Shibuya K, Kodera Y, Fujii T: Prognostic factors in conversion surgery following nab-paclitaxel with gemcitabine and subsequent chemoradiotherapy for unresectable locally advanced pancreatic cancer: Results of a dual-center study. Ann Gastroenterol Surg 7(1): 157-166, 2023. DOI: 10.1002/ags3.12613

88 Jiang P, Li X, Wang S, Liu Y: Prognostic significance of PNI in patients with pancreatic head cancer undergoing laparoscopic pancreaticoduodenectomy. Front Surg 9: 897033, 2022. DOI: 10.3389/fsurg.2022.897033

89 Frigerio I, Malleo G, de Pastena M, Deiro G, Surci N, Scopelliti F, Esposito A, Regi P, Giardino A, Allegrini V, Bassi C, Girelli R, Salvia R, Butturini G: Prognostic factors after pancreatectomy for pancreatic cancer initially metastatic to the liver. Ann Surg Oncol 29(13): 8503-8510, 2022. DOI: 10.1245/s10434-022-12385-4

90 Yang L, Su J, Wang W, Zhou F: The efficacy and safety of Nab-paclitaxel plus gemcitabine versus mFOLFIRINOX in the first-line treatment of metastatic pancreatic cancer: a retrospective study. World J Surg Oncol 21(1): 19, 2023. DOI: 10.1186/s12957-023-02896-z

91 Ikeguchi M, Hanaki T, Endo K, Suzuki K, Nakamura S, Sawata T, Shimizu T: C-reactive protein/albumin ratio and prognostic nutritional index are strong prognostic indicators of survival in resected pancreatic ductal adenocarcinoma. J Pancreat Cancer 3(1): 31-36, 2017. DOI: 10.1089/pancan.2017.0006

92 Liu Z, Jin K, Guo M, Long J, Liu L, Liu C, Xu J, Ni Q, Luo G, Yu X: Prognostic value of the CRP/Alb ratio, a novel inflammation-based score in pancreatic cancer. Ann Surg Oncol 24(2): 561-568, 2017. DOI: 10.1245/s10434-016-5579-3

93 Ikeguchi M, Hanaki T, Endo K, Suzuki K, Nakamura S, Sawata T, Shimizu T: C-reactive protein/albumin ratio and prognostic nutritional index are strong prognostic indicators of survival in resected pancreatic ductal adenocarcinoma. J Pancreat Cancer 3(1): 31-36, 2017. DOI: 10.1089/pancan.2017.0006

94 Hang J, Xue P, Yang H, Li S, Chen D, Zhu L, Huang W, Ren S, Zhu Y, Wang L: Pretreatment C-reactive protein to albumin ratio for predicting overall survival in advanced pancreatic cancer patients. Sci Rep 7(1): 2993, 2017. DOI: 10.1038/s41598-017-03153-6

95 Liu Z, Jin K, Guo M, Long J, Liu L, Liu C, Xu J, Ni Q, Luo G, Yu X: Prognostic value of the CRP/Alb ratio, a novel inflammation-based score in pancreatic cancer. Ann Surg Oncol 24(2): 561-568, 2017. DOI: 10.1245/s10434-016-5579-3

96 Ikuta S, Aihara T, Yamanaka N: Preoperative C-reactive protein to albumin ratio is a predictor of survival after pancreatic resection for pancreatic ductal adenocarcinoma. Asia Pac J Clin Oncol 15(5): e109-e114, 2019. DOI: 10.1111/ajco.13123

97 Kim HJ, Lee SY, Kim DS, Kang EJ, Kim JS, Choi YJ, Oh SC, Seo JH, Kim JS: Inflammatory markers as prognostic indicators in pancreatic cancer patients who underwent gemcitabine-based palliative chemotherapy. Korean J Intern Med 35(1): 171-184, 2020. DOI: 10.3904/kjim.2018.076

98 van Wijk L, de Klein GW, Kanters MA, Patijn GA, Klaase JM: The ultimate preoperative C-reactive protein-to-albumin ratio is a prognostic factor for survival after pancreatic cancer resection. Eur J Med Res 25(1): 46, 2020. DOI: 10.1186/s40001-020-00444-z

99 Mori S, Aoki T, Sakuraoka Y, Shimizu T, Yamaguchi T, Park K, Matsumoto T, Shiraki T, Iso Y, Kubota K: Predictors of poor pathological response to neoadjuvant gemcitabine plus S-1 chemotherapy in patients with pancreatic ductal adenocarcinoma. Pancreas 50(5): 744-750, 2021. DOI: 10.1097/MPA.0000000000001826

100 Terao T, Kumagi T, Hyodo I, Yokota T, Azemoto N, Miyata H, Kuroda T, Ohno Y, Tanaka Y, Shibata N, Imamura Y, Kanemitsu K, Miyake T, Koizumi M, Hiasa Y, Ehime Pancreato-Cholangiology (EPOCH) Study Group: Simple prognostic markers for optimal treatment of patients with unresectable pancreatic cancer. Medicine (Baltimore) 100(43): e27591, 2021. DOI: 10.1097/MD.0000000000027591

101 Funamizu N, Sogabe K, Shine M, Honjo M, Sakamoto A, Nishi Y, Matsui T, Uraoka M, Nagaoka T, Iwata M, Ito C, Tamura K, Sakamoto K, Ogawa K, Takada Y: Association between the preoperative c-reactive protein-to-albumin ratio and the risk for postoperative pancreatic fistula following distal pancreatectomy for pancreatic cancer. Nutrients 14(24): 5277, 2022. DOI: 10.3390/nu14245277

102 Kato Y, Yamada S, Suenaga M, Takami H, Niwa Y, Hayashi M, Iwata N, Kanda M, Tanaka C, Nakayama G, Koike M, Fujiwara M, Kodera Y: Impact of the controlling nutritional status score on the prognosis after curative resection of pancreatic ductal adenocarcinoma. Pancreas 47(7): 823-829, 2018. DOI: 10.1097/MPA.0000000000001105

103 Wang A, Sun B, Wang M, Shi H, Huang Z, He T, Li Q, Deng J, Fu W, Jiang Y: Predictive value of CONUT score combined with serum CA199 levels in postoperative survival of patients with pancreatic ductal adenocarcinoma: a retrospective study. PeerJ 8: e8811, 2020. DOI: 10.7717/peerj.8811

104 Shiihara M, Higuchi R, Izumo W, Yazawa T, Uemura S, Furukawa T, Yamamoto M: Impact of the controlling nutritional status score on severe postoperative complications of pancreaticoduodenectomy for pancreatic cancer. Langenbecks Arch Surg 406(5): 1491-1498, 2021. DOI: 10.1007/s00423-021-02151-7

105 Terasaki F, Sugiura T, Okamura Y, Ito T, Yamamoto Y, Ashida R, Ohgi K, Uesaka K: The preoperative controlling nutritional status (CONUT) score is an independent prognostic marker for pancreatic ductal adenocarcinoma. Updates Surg 73(1): 251-259, 2021. DOI: 10.1007/s13304-020-00792-9

106 Uemura S, Iwashita T, Ichikawa H, Iwasa Y, Mita N, Shiraki M, Shimizu M: Impact of Controlling nutritional status (CONUT) in patients with unresectable advanced pancreatic cancer receiving multi-agent chemotherapy: A single center, retrospective cohort study. Pancreatology 22(2): 304-310, 2022. DOI: 10.1016/j.pan.2022.01.010

107 Dang C, Wang M, Zhu F, Qin T, Qin R: Controlling nutritional status (CONUT) score-based nomogram to predict overall survival of patients with pancreatic cancer undergoing radical surgery. Asian J Surg 45(6): 1237-1245, 2022. DOI: 10.1016/j.asjsur.2021.08.011

108 Shirai Y, Shiba H, Sakamoto T, Horiuchi T, Haruki K, Fujiwara Y, Futagawa Y, Ohashi T, Yanaga K: Preoperative platelet to lymphocyte ratio predicts outcome of patients with pancreatic ductal adenocarcinoma after pancreatic resection. Surgery 158(2): 360-365, 2015. DOI: 10.1016/j.surg.2015.03.043

109 Li W, Chen Y, Wang X, Shi Y, Dai G, Li X: Pretreatment platelet to lymphocyte ratio is predictive of overall survival in metastatic pancreatic ductal adenocarcinoma. Transl Cancer Res 8(1): 17-22, 2019. DOI: 10.21037/tcr.2018.12.20

110 Hoshimoto S, Hishinuma S, Shirakawa H, Tomikawa M, Ozawa I, Ogata Y: Validation and clinical usefulness of pre- and postoperative systemic inflammatory parameters as prognostic markers in patients with potentially resectable pancreatic cancer. Pancreatology 20(2): 239-246, 2020. DOI: 10.1016/j.pan.2019.12.004

111 Kim HJ, Lee SY, Kim DS, Kang EJ, Kim JS, Choi YJ, Oh SC, Seo JH, Kim JS: Inflammatory markers as prognostic indicators in pancreatic cancer patients who underwent gemcitabine-based palliative chemotherapy. Korean J Intern Med 35(1): 171-184, 2020. DOI: 10.3904/kjim.2018.076

112 Schlanger D, Popa C, Pașca S, Seicean A, Al Hajjar N: The role of systemic immuno-inflammatory factors in resectable pancreatic adenocarcinoma: a cohort retrospective study. World J Surg Oncol 20(1): 144, 2022. DOI: 10.1186/s12957-022-02606-1

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