Original Article

Prognostic Values of Systemic Immune-inflammation (SII) Index and Systemic Inflammatory Markers in Advanced Stage Solid Tumor Patients Received Palliative Chemotherapy

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Background: The systemic inflammatory response can be reflected by hematological parameters, including the neutrophil-to-lymphocyte ratio (NLR), the monocyte-to-lymphocyte ration (MLR) and the platelet-to-lymphocyte ration (PLR). A new inflammatory index, called systemic immune-inflammatory index (SII) has been recently suggested to be associated with poor survival outcomes in many cancers. However, there is no study of SII index and inflammatory marker demonstrated survival outcomes and response of chemotherapy in advanced staged solid tumor. Therefore, these questions are necessary to evaluate the prognostic value of SII index and inflammatory markers.

Objective: The present study was performed to investigation the prognostic role of these marker index in this setting.

Materials and Methods: The authors retrospectively analyzed 354 patients who diagnosed advanced stage or recurrent disease of cancer patients who received palliative chemotherapy between 2014 and 2019. Patients clinicopathological parameters were recorded. The authors calculated inflammatory-based biomarker (SII index, NLR, MLR and PLR) and analyzed correlation of SII index and systemic inflammatory markers as prognosis value in term of progression free survival (PFS) and overall survival (OS).

Results: The 354 patients were included in the present study. Most of the tumor types were primary lung cancer (42.9%), breast cancer (16.1%) and colorectal cancer (14.1%). A high SII index was correlated with good PFS (HR = 0.998), p-value = 0.019. While high NLR, MLR and PLR were correlated with poor PFS (HR = 1.036, 2.024 and 1.015), p-value = 0.007, 0.001 and <0.001, respectively. Likewise, overall survival outcome had the same correlation result. ROC curves determine the same values of these inflammatory markers as prediction prognosis.

Conclusion: SII index, NLR, MLR and PLR are prognostic predictor in advanced stage solid tumor patients received chemotherapy. Higher SII index might be good prognosis marker in these setting. The low cost, feasible and reproducibility of these markers may be helpful as a prognostic tool.

Keywords: Advance cancer; Chemotherapy; Inflammatory markers; SII; NLR; MLR; PLR

J Med Assoc Thai 2022;105(Suppl.1): S50-7
Website: http://www.jmatonline.com

Cancer is the most cause of death in Thailand and worldwide. Globally, an almost one-in-six death is due to cancer[1]. Cancer is a group of diseases which can influence any part of the body. Recurrence and metastasis are poor prognosis outcomes and survival. Mainstay of therapy in advanced stage solid tumor is palliative chemotherapy. Currently, targeted therapy and immunotherapy can improve survival outcomes in these patients but reimbursement to these high-cost therapies are limit in Lower to middle outcome country. Palliative chemotherapy is still be a valuable therapy for these setting. Therefore, identifying better predictors for prognosis and response in advanced stage solid tumor patients with palliative chemotherapy are important.

The correlation between chronic inflammation and cancer has been experimented by many studies[2,3]. Chronic inflammation affects all stage of cancer, increasing the risk, supporting the initial genetic mutation and epigenetic mechanism leading to cancer[4-6], promoting tumor progression and metastasis[7-10]. The systemic inflammatory response is involved in the progression, response of treatment and prognosis of many cancers[11]. The systemic inflammatory response can be reflected by hematological parameters, including the neutrophil-to-lymphocyte ratio (NLR), the

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How to cite this article:
Munthum D, Phirom S, Charonpongsuntorn C. Prognostic Values of Systemic Immune-inflammation (SII) Index and Systemic Inflammatory Markers in Advanced Stage Solid Tumor Patients Received Palliative Chemotherapy. J Med Assoc Thai 2022;105 (Suppl.1): S50-7.
doi.org/10.35755/jmedassocthai.2022.S01.00023

monocyte-to-lymphocyte ration (MLR) and the platelet-to-lymphocyte ration (PLR). Many studies have shown association of inflammatory parameter with poor prognosis of cancers[12-15], and some evidences has revealed an association of systemic inflammation and resistance to chemotherapy[16,17]. A new inflammatory index, based on neutrophil, platelet and lymphocyte counts called systemic immune-inflammatory index (SII) has been recently suggested to be associated with poor survival outcomes in many cancers, including hepatocellular carcinoma, esophageal cancer, small lung cancer and non-small cell lung cancer[18-21]. Recently, controversy result of many studies are needed to explore contrary views[22,23]. SII index has demonstrated response of treatment with chemotherapy and epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor and outcomes in non-small cell lung carcinoma[24,25].

However, there is no study of SII index and inflammatory marker demonstrating survival outcomes and response of chemotherapy in advanced stage solid tumor in Thailand. Therefore, these questions are necessary to evaluate the prognostic value of SII index and inflammatory markers. Then, the present study was performed to investigation the prognostic role of these marker index in this setting.

Materials and Methods

In the present study, we retrospectively analyzed 354 patients who diagnosed advanced stage or recurrent disease of cancer patients who received palliative chemotherapy between 2014 and 2019. We included recurrent or advanced stage solid tumors and palliative chemotherapy is systemic therapy. Exclusion criteria were hematologic malignancy, hematologic disease, HIV infection, autoimmune disease and patients who received Granulocyte colony stimulating factor (G-CSF). Incomplete or inaccurate data and pretreatment blood examination before chemotherapy were excluded. Patient with active infection or sepsis was excluded. Tumor stage was determined according to American Joint Committee on Cancer TNM staging system. Patients clinicopathological parameters were recorded, including age, gender, type of primary cancer, Eastern Cooperative Oncology Group (ECOG) performance status, Receiving of palliative chemotherapy, Response of chemotherapy by Response evaluation criteria in solid tumor (RECIST) version 1.1 and routing blood results. These parameters were obtained from medical records and electronic medical document. The laboratory test was collected at first cycles of chemotherapy.

Primary objective is role of SII index and systemic inflammatory markers as prognosis value in term of progression free survival (PFS) and overall survival (OS) in recurrent and advanced stage solid tumor with palliative chemotherapy. Secondary outcome is clinical correlation, cut-off finding and useful of these biomarkers as prognosis biomarker. The study followed the guidelines of the Helsinki declaration and was approved by the Ethics Committee of Strategic Wisdom and Research Institute, Srinakharinwirot University (SWUEC/E-163/2563). Informed consent was exempted for this retrospective study.

Definition of inflammation-based biomarker

Complete blood count data were analyzed in general laboratory within one week before chemotherapy. We calculated the SII index, NLR, MLR and PLR as follows: SII = platelet count x neutrophil count/lymphocyte count[26], NLR = neutrophil count/lymphocyte count, MLR = monocyte count/lymphocyte count and PLR = platelet count/lymphocyte count.

Sample size calculation

Review study of SII index as predictive biomarker for progression of disease in Non-small cell lung carcinoma who received chemotherapy found that SII less than 1,270 has prolong progression free survival at 5.2 months compared to 3.3 months in SII more than 1,270[24]. We calculated sample size estimation for time to event data based on median survival time with accrual data collection time at 3 years and follow-up time at 2 years. Type I error = 0.05 and Power = 0.8. Power and Sample size calculation estimated sample size with 354 patients in the present study.

Statistical analysis

The statistic package for Social Science (SPSS, version 23.0) were used to perfom the statistical analyses. Descriptive statistic were used to summarize the characteristics and the distribution of CBC-based predictors. Chi-squared or Fisher's exact test was used to access the categorical variable. The Kaplan-Meier method and log-rank test were performed to evaluate the survival outcomes, including PFS and OS. We used the Cox proportional hazard model for univariate analyses, and hazard ration (HRs) with 95% confidence intervals (CI) were used to quantify the prognostic value of the predictors. A two-sided value of $p<0.05$ was considered statistically significant. We construted receiver operating characteristic (ROC) curves to determine the optional cutoff values for the SII index, NLR, MLR and PLR that yielded the maximum joint sensitivity and specificity.

Results

Patient characteristics

The 354 patients included in the present study consisted of 183 (51.7%) men and 171 (48.3%) women (Table 1). The median age was 62.4 years. Most of the tumor types were primary lung cancer 152 patients (42.9%), breast cancer 57 patients (16.1%) and colorectal cancer 50 patients (14.1%). ECOG performance status was PS 0, 42 patients (11.9%); PS 1, 201 patients (57.0%); PS 2, 59 patients (16.7%) and PS 3 to 4, 51 patients (14.4%). All of patients in the present study have received palliative chemotherapy. Mostly, Best response of chemotherapy was progressive disease, 135 patients (38.1%); partial response, 112 patients (31.7%) and stable disease, 107 patients (30.2%). There is

Table 1. Baseline Patient Characteristics

Variables	Number (percentage) (n=354)	High SII (n=190)	Low SII (n=164)
Sex			
Male	183 (51.7%)	92 (48.4)	91 (51.7)
Female	171 (48.3%)	98 (51.6)	73 (48.3)
Age (mean, SD)	62.4 (12.9)	61.4 (12.8)	63.7 (13.1)
Primary cancer			
Lung cancer	152 (42.9%)	81 (42.7)	71 (42.9)
Breast cancer	57 (16.1%)	31 (16.3)	26 (15.8)
Colorectal cancer	50 (14.1%)	26 (13.7)	24 (14.6)
Hepatocellular carcinoma	9 (2.5%)	3 (1.6)	6 (3.7)
Cholangiocarcinoma	26 (7.3%)	15 (7.9)	11 (6.7)
Stomach cancer	12 (3.4%)	6 (3.2)	6 (3.2)
Pancreatic cancer	19 (5.4%)	10 (5.3)	9 (5.5)
Cervical cancer	2 (0.6%)	1 (0.5)	1 (0.5)
Germ cell tumor	1 (0.3%)	1 (0.5)	-
Skin cancer	2 (0.6%)	2 (1.0)	-
Bone and soft tissue malignancy	2 (0.6%)	1 (0.5)	1 (0.5)
Others	22 (6.2%)	13 (6.8)	9 (2.5)
ECOG			
0	42 (11.9%)	24 (12.6)	18 (11.0)
1	202 (57.0%)	112 (58.9)	90 (54.9)
2	59 (16.7%)	31 (16.3)	28 (17.1)
3	40 (11.3%)	16 (8.4)	24 (14.6)
4	11 (3.1%)	7 (3.7)	4 (2.4)
Chemotherapy			
Yes	354 (100%)	-	-
No	0		
Response to chemotherapy			
Complete response (CR)	0	-	-
Partial response (PR)	112 (31.7%)	61 (32.1)	51 (31.1)
Stable disease (SD)	107 (30.2%)	62 (32.6)	45 (27.4)
Progressive disease (PD)	135 (38.1%)	67 (35.3)	68 (41.5)
Hematocrit			
Mean (%) (SD)	36 (1.6)	36 (1.7)	34 (1.9)
White blood cell (SD)			
Mean (/mm^3)	9,102 (4,626)	7,525 (2,575)	9,375 (5,925)
Neutrophile (mean %)	66.5 (11.8)	59.7 (9.7)	74.3 (8.7)
Lymphocyte (mean %)	22.7 (10.0)	28.6 (8.4)	15.8 (6.7)
Monocyte (mean %)	6.1 (2.4)	6.1 (2.1)	6.1 (2.7)
Eosinophil (mean %)	2.8 (3.3)	3.4 (3.5)	2.3 (2.9)
Platelet (SD)			
Mean (/mm^3)	348,333 (144,469)	375,968 (150,364)	316,317 (130,623)

no complete remission in the present study. At baseline, the median pre-treatment Hematocrit, white blood cell count and platelet count were, 36%, 9,102/mm^3 and 348,333/mm^3, respectively. Median differentiation of white blood cell count, neutrophil, lymphocyte and monocyte were 66.5%, 22.7% and 6.1%, respectively. Median follow-up time was

2.62 years (0.04 to 8.91).

Correlation between survival outcome (progression free survival and overall survival) and SII index and systemic inflammatory markers

We used the Kaplan-Meier method to analyze the progression free survival and overall survival and compared them using the log-rank test. A high SII index was correlated with good PFS (HR = 0.998), p-value = 0.019. While high NLR, MLR and PLR were correlated with poor PFS (HR = 1.036, 2.024 and 1.015), p-value = 0.007, 0.001 and <0.001, respectively. Likewise, overall survival outcome had the same correlation result. A high SII index was correlated with prolong OS (HR = 0.998), p-value = 0.026. While high NLR, MLR and PLR were correlated with poor OS (HR = 1.036, 1.367 and 1.018), p-value = 0.005, 0.143 and <0.001, respectively (Table 2). Univariate analysis showed that ECOG, primary tumor type and SII with systemic inflammatory markers were factors that correlated with survival outcome. Multivariate analysis was analyzed and shown that primary tumor type and SII with systemic inflammatory markers were factors that significantly correlated PFS and OS except MLR (Table 2).

Subgroup analysis stratified by tumor type (lung cancer, breast cancer and colorectal cancer). We found that high SII index was correlated with prolong PFS and OS. In contrast, high NLR, MLR and PLR were correlated with shorten PFS and OS. High SII index was statistically significant correlated with prolong PFS in lung cancer (HR = 0.998, p-value = 0.033) but high PLR was statistically significant correlated with poor PFS (HR = 1.010, p-value = 0.047). Breast cancer and colorectal cancer had statistically significant correlation with high MLR and poor outcomes (Table 3).

Selection of optimal cutoff value for SII index, NLR, MLR and PLR

Previous studies have suggested different cutoff values when analyzing the prognostic value of SII index and systemic inflammatory markers. In the present study, we constructed ROC curves to determine the optimal cutoff values. As shown in Figure 1, the areas under ROC curves (AUCs) were 0.56, 0.59, 0.54 and 0.53 for the SII index, NLR, MLR and PLR, respectively. The optimal cutoff values for prediction of overall survival were 100 for the SII index, 2.8 for the NLR, 0.25 for the MLR and 12 for the PLR with sensitivity and specificity result in Table 4.

Prognosis values of SII index, NLR, MLR and PLR

We used the Kaplan-Meier method to analyze the overall survival and compared them using the log-rank test. We separated the patients into two groups according to the optimal cutoff values. The result shown statistically significant correlation with prolonged OS and high SII index and low NLR, MLR and PLR. Hazard ratio = 1.41 (1.12 to 1.78), 1.66 (1.31 to 2.10), 1.32 (1.05 to 1.68) and 1.29 (1.02 to 1.64), respectively (Figure 2).

Discussion

In context of low to middle income countries which have limitation in reimbursement of high-cost drug such as target therapy or immunotherapy. These setting can be used only palliative chemotherapy and we do not have the handily, feasible and economical prognostic biomarkers. Our research questions are evaluation of the prognostic biomarkers in this setting. The systemic inflammatory markers had correlation with poor prognosis of cancers and response of chemotherapy. A new novel marker, SII index has never been explored in these population. Therefore, these questions are necessary to evaluation the prognostic value of SII index and systemic inflammatory markers.

There is no data of SII index and inflammatory marker demonstrating survival outcomes and response of chemotherapy in advanced stage solid tumor in Thailand. This study performed to investigation the prognostic role of these marker index in this setting. To the best of our knowledge, compared to previous studies, our sample included the largest population of patients with advanced stage or recurrent disease. Our study focused exclusively on the prognostic values of the SII index and systemic inflammatory markers, including NLR, MLR and PLR in patients who received only palliative chemotherapy that compatible with context of low to middle income countries.

We showed that systemic inflammatory markers

Table 2. Association of SII index, NLR, MLR and PLR with survival outcomes in advanced stage solid tumor patients received palliative chemotherapy

Survival outcome	Index	Crude HR (95% CI)	p-value	Adjust HR (95% CI)	p-value
Progression free survival (PFS)	SII	0.998 (0.996 to 0.999)	0.019	0.998 (0.996 to 0.999)	<0.009
	NLR	1.036 (1.009 to 1.058)	0.007	1.031 (1.005 to 1.059)	0.018
	MLR	2.024 (1.329 to 3.063)	0.001	1.357 (0.886 to 2.076)	0.159
	PLR	1.015 (1.005 to 1.014)	<0.001	1.007 (1.002 to 1.012)	0.003
Overall survival (OS)	SII	0.998 (0.996 to 0.999)	0.026	0.998 (0.996 to 0.999)	0.007
	NLR	1.036 (1.010 to 1.062)	0.005	1.032 (1.007 to 1.057)	0.010
	MLR	1.367 (0.900 to 2.074)	0.143	1.938 (1.259 to 2.984)	0.003
	PLR	1.008 (1.003 to 1.013)	<0.001	1.010 (1.005 to 1.015)	<0.001

Table 3. Association of SII index, NLR, MLR and PLR with survival outcomes in advanced stage lung, breast and colorectal cancer patients received palliative chemotherapy

Primary organ	Survival outcome	Index	HR (95% CI)	p-value
Lung cancer	Progression free survival (PFS)	SII	0.998 (0.995 to 0.998)	0.033
		NLR	1.011 (0.978 to 1.052)	0.430
		MLR	1.341 (0.743 to 2.443)	0.325
		PLR	1.010 (1.000 to 1.016)	0.047
	Overall survival (OS)	SII	0.998 (0.995 to 1.000)	0.061
		NLR	1.001 (0.970 to 1.048)	0.645
		MLR	1.186 (0.668 to 2.104)	0.561
		PLR	1.002 (0.996 to 1.012)	0.264
Breast cancer	Progression free survival (PFS)	SII	0.998 (0.991 to 1.003)	0.457
		NLR	1.027 (0.924 to 1.137)	0.636
		MLR	4.495 (0.508 to 39.808)	0.177
		PLR	1.003 (0.982 to 1.022)	0.799
	Overall survival (OS)	SII	0.998 (0.990 to 1.004)	0.478
		NLR	1.074 (0.952 to 1.218)	0.238
		MLR	21.78 (1.473 to 322.23)	0.025
		PLR	1.003 (0.981 to 1.032)	0.597
Colorectal cancer	Progression free survival (PFS)	SII	0.998 (0.994 to 1.000)	0.169
		NLR	1.024 (0.943 to 1.110)	0.568
		MLR	5.495 (1.245 to 24.208)	0.024
		PLR	1.002 (0.985 to 1.017)	0.859
	Overall survival (OS)	SII	1.001 (0.997 to 1.004)	0.725
		NLR	1.023 (0.919 to 1.140)	0.666
		MLR	0.794 (0.191 to 3.330)	0.758
		PLR	1.012 (0.993 to 1.030)	0.214

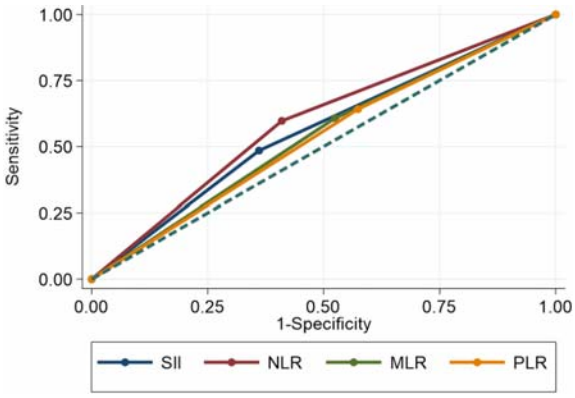

Figure 1. Receiver operating characteristics (ROC) curve analysis of the optimal cutoff values of SII index, NLR, MLR and PLR.

evaluated by SII index, NLR, MLR and PLR, could act as an effective marker to predict the prognosis of advanced stage or recurrent cancer patients with chemotherapy. Moreover, all of them were further confirmed by ROC analysis and predicted survival outcomes. Comparison of the AUCs showed that the prognostic ability of the SII index and systemic inflammatory markers was the same. The low SII index and high NLR, MLR and PLR had correlation with poor survival outcomes.

Cancer-related inflammation in the tumor microenvironment and inflammatory cells in the circulation may play important roles in tumor progression[6]. In recent years, many studies have shown association of inflammatory parameter with poor prognosis of cancers[12-15]. The high NLR, MLR and PLR values correlate with poor prognosis[27-29]. But previous studies were focused on some type of cancers and treatment with surgery or radiation therapy[12-14,16]. We confirmed the useful of these prognostic values in our study that these inflammatory markers can be useful to predict survival outcomes in advanced stage solid tumor with palliative chemotherapy.

Although, several studies reported the SII index, which is based on neutrophils, platelet counts and lymphocytes, seem to be a stronger prognostic predictor in variety of solid tumors including lung cancer[30-32]. However, our studies revealed SII index was protective effect to predicted survival outcomes in small number of hazard ratio (HR = 0.998) but significant in term of statistics. These finding was contrast with previous studies. The mechanism by which a high SII index value contributing to poor prognosis for cancer patients remains unclear. Based on higher SII may be association with tumor angiogenesis, invasion and metastasis thus leading to poor survival[33]. These finding may be explained due to our study including only advanced

Table 4. Receiver operating characteristics (ROC) analyses of SII, NLR, MLR and PLR in Advanced stage solid tumor patient who received chemotherapy

Parameters	Cut-off value	AUC (95% CI)	Sensitivity	Specificity
SII	100	0.56 (0.49 to 0.63)	48.5%	63.9%
NLR	2.8	0.59 (0.52 to 0.66)	59.7%	59%
MLR	0.25	0.54 (0.47 to 0.61)	60.8%	47.5%
PLR	12	0.53 (0.46 to 0.60)	64.2%	42.6%

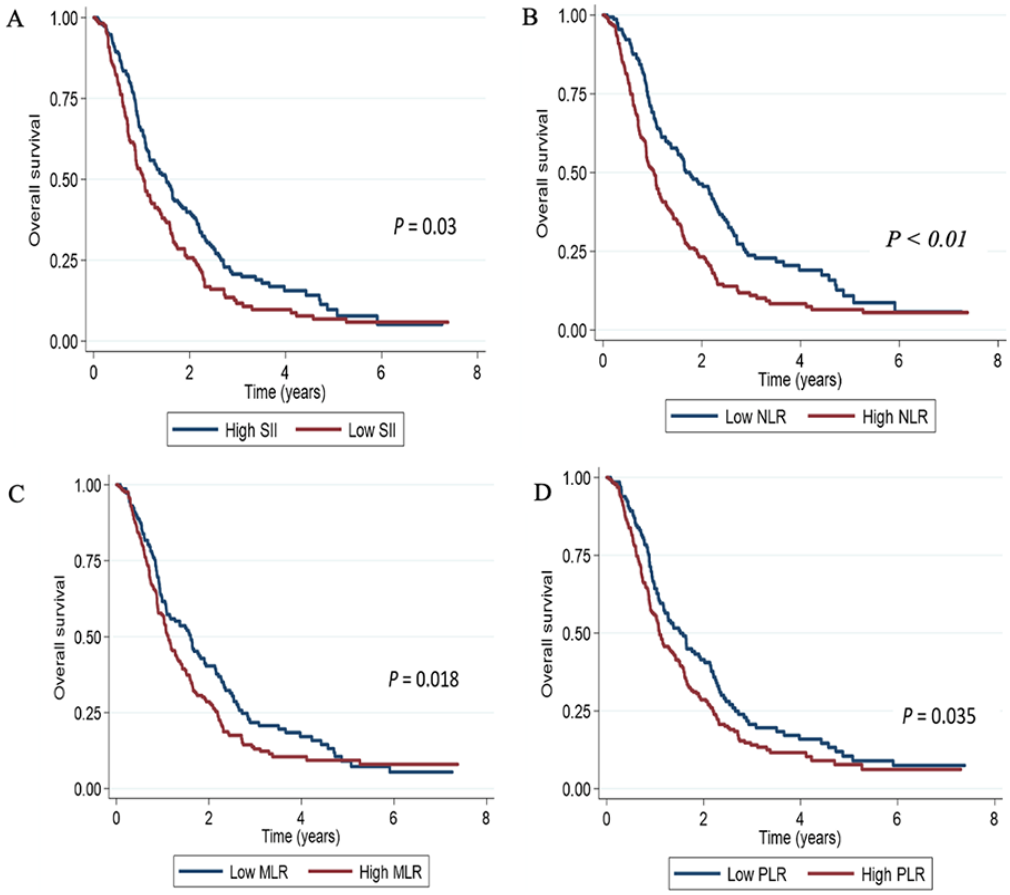

Figure 2. Kaplan-Meier overall survival curve according to (A) the SII index (B) NLR (C) MLR and (D) PLR.

stage of cancers that have poor prognosis and all types of cancers which was more heterogeneity. Large scale prospective and specificity in some population and type of cancer are also needed to be performed to confirm the conclusion.

Nevertheless, there were several limitations in our study. First, the present study is retrospective nature data, our study may have been subject to selection bias. Second, we included all type of cancers, variable of chemotherapy and performance status which was more heterogeneity. To our knowledge, the strengths of our study was the first study of inflammatory markers in prediction of survival outcome with palliative chemotherapy and large number of population and technically of statistical analysis that show the benefit of these valuable prognostic markers that can be easily, feasible and useful in our setting. Prospective studies with specific population are needed to explore in the future.

Conclusion

The systemic inflammatory markers including SII index, NLR, MLR and PLR are prognostic predictor in advanced stage solid tumor patients received chemotherapy. Higher SII index might be protective marker in these setting. The low cost, feasible and reproducibility of these systemic inflammatory markers may be helpful as a prognostic tool for assessing advanced cancer prognosis.

What is already known on this topic?

The systemic inflammatory markers had correlation with poor prognosis of cancers and response of chemotherapy. A new novel marker, SII index has never been explored in these population. Therefore, these questions are necessary to evaluate the prognostic value of SII index and systemic inflammatory markers.

What this study adds?

The systemic inflammatory markers including SII index, NLR, MLR and PLR may be useful as prognostic predictor in advanced stage solid tumor patients received chemotherapy. Higher SII index might be protective marker in these setting.

Acknowledgements

The authors would like to thank all colleagues in the Department of Internal Medicine, Faculty of Medicine, Srinakharinwirot University. Finally, the authors were most appreciated for the participation of all patients in this research.

Potential conflicts of interest

The authors declare no conflict of interests.

References

1. World Health Organization. Fact sheet: Cancer [Internet]. 2017 [cited 2017 Feb 1]. Available from: http://www.who.int/mediacentre/factsheets/fs297/en/.
2. Coussens LM, Werb Z. Inflammation and cancer. Nature 2002;420:860-7.
3. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature 2008;454:436-44.
4. Hussain SP, Hofseth LJ, Harris CC. Radical causes of cancer. Nat Rev Cancer 2003;3:276-85.
5. Colotta F, Allavena P, Sica A, Garlanda C, Mantovani A. Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability. Carcinogenesis 2009;30:1073-81.
6. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell 2010;140:883-99.
7. Aggarwal BB, Gehlot P. Inflammation and cancer: how friendly is the relationship for cancer patients? Curr Opin Pharmacol 2009;9:351-69.
8. Multhoff G, Molls M, Radons J. Chronic inflammation in cancer development. Front Immunol 2011;2:98.
9. De Lerma Barbaro A, Perletti G, Bonapace IM, Monti E. Inflammatory cues acting on the adult intestinal stem cells and the early onset of cancer (review). Int J Oncol 2014;45:959-68.
10. Ostan R, Lanzarini C, Pini E, Scurti M, Vianello D, Bertarelli C, et al. Inflammaging and cancer: a challenge for the Mediterranean diet. Nutrients 2015;7:2589-621.
11. Karki R, Man SM, Kanneganti TD. Inflammasomes and Cancer. Cancer Immunol Res 2017;5:94-9.
12. Huang QT, Zhou L, Zeng WJ, Ma QQ, Wang W, Zhong M, et al. Prognostic significance of neutrophil-to-lymphocyte ratio in ovarian cancer: A systematic review and meta-analysis of observational studies. Cell Physiol Biochem 2017;41:2411-8.
13. Zhou WJ, Wu J, Li XD, Wang Q, Ni XF, Jiang JT, et al. [Effect of preoperative monocyte-lymphocyte ratio on prognosis of patients with resectable esophagogastric junction cancer]. Zhonghua Zhong Liu Za Zhi 2017;39:178-83.
14. Cummings M, Merone L, Keeble C, Burland L, Grzelinski M, Sutton K, et al. Preoperative neutrophil:lymphocyte and platelet:lymphocyte ratios predict endometrial cancer survival. Br J Cancer 2015;113:311-20.
15. Zheng Z, Zhou L, Gao S, Yang Z, Yao J, Zheng S. Prognostic role of C-reactive protein in hepatocellular carcinoma: a systematic review and meta-analysis. Int J Med Sci 2013;10:653-64.
16. Stotz M, Pichler M, Absenger G, Szkandera J, Arminger F, Schaberl-Moser R, et al. The preoperative lymphocyte to monocyte ratio predicts clinical outcome in patients with stage III colon cancer. Br J Cancer 2014;110:435-40.
17. Wu Q, Hu T, Zheng E, Deng X, Wang Z. Prognostic role of the lymphocyte-to-monocyte ratio in colorectal cancer: An up-to-date meta-analysis. Medicine (Baltimore) 2017;96:e7051.
18. Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res 2014;20:6212-22.
19. Geng Y, Shao Y, Zhu D, Zheng X, Zhou Q, Zhou W, et al. Systemic immune-inflammation index predicts prognosis of patients with esophageal squamous cell carcinoma: A propensity score-matched analysis. Sci Rep 2016;6:39482.
20. Hong X, Cui B, Wang M, Yang Z, Wang L, Xu Q. Systemic immune-inflammation index, based on platelet counts and neutrophil-lymphocyte ratio, is useful for predicting prognosis in small cell lung cancer. Tohoku J Exp Med 2015;236:297-304.
21. Guo D, Zhang J, Jing W, Liu J, Zhu H, Fu L, et al. Prognostic value of systemic immune-inflammation index in patients with advanced non-small-cell lung cancer. Future Oncol 2018;14:2643-50.
22. Gao XH, Tian L, Wu J, Ma XL, Zhang CY, Zhou Y, et al. Circulating CD14(+) HLA-DR(-/low) myeloid-derived suppressor cells predicted early recurrence of

hepatocellular carcinoma after surgery. Hepatol Res 2017;47:1061-71.
23. Liu X, Sun X, Liu J, Kong P, Chen S, Zhan Y, et al. Preoperative C-reactive protein/albumin ratio predicts prognosis of patients after curative resection for gastric cancer. Transl Oncol 2015;8:339-45.
24. Berardi R, Santoni M, Rinaldi S, Bower M, Tiberi M, Morgese F, et al. Pre-treatment systemic immune-inflammation represents a prognostic factor in patients with advanced non-small cell lung cancer. Ann Transl Med 2019;7:572.
25. Deng C, Zhang N, Wang Y, Jiang S, Lu M, Huang Y, et al. High systemic immune-inflammation index predicts poor prognosis in advanced lung adenocarcinoma patients treated with EGFR-TKIs. Medicine (Baltimore) 2019;98:e16875.
26. Wang K, Diao F, Ye Z, Zhang X, Zhai E, Ren H, et al. Prognostic value of systemic immune-inflammation index in patients with gastric cancer. Chin J Cancer 2017;36:75.
27. Guo J, Chen S, Chen Y, Li S, Xu D. Combination of CRP and NLR: a better predictor of postoperative survival in patients with gastric cancer. Cancer Manag Res 2018;10:315-21.
28. Feng JF, Huang Y, Chen QX. Preoperative platelet lymphocyte ratio (PLR) is superior to neutrophil lymphocyte ratio (NLR) as a predictive factor in patients with esophageal squamous cell carcinoma. World J Surg Oncol 2014;12:58.
29. Luo H, Ge H, Cui Y, Zhang J, Fan R, Zheng A, et al. Systemic inflammation biomarkers predict survival in patients of early stage non-small cell lung cancer treated with stereotactic ablative radiotherapy - a single center experience. J Cancer 2018;9:182-8.
30. Tomita M, Ayabe T, Maeda R, Nakamura K. Systemic immune-inflammation index predicts survival of patients after curative resection for non-small cell lung cancer. In Vivo 2018;32:663-7.
31. Tong YS, Tan J, Zhou XL, Song YQ, Song YJ. Systemic immune-inflammation index predicting chemoradiation resistance and poor outcome in patients with stage III non-small cell lung cancer. J Transl Med 2017;15:221.
32. Gao Y, Zhang H, Li Y, Wang D, Ma Y, Chen Q. Preoperative increased systemic immune-inflammation index predicts poor prognosis in patients with operable non-small cell lung cancer. Clin Chim Acta 2018;484:272-7.
33. Gooden MJ, de Bock GH, Leffers N, Daemen T, Nijman HW. The prognostic influence of tumour-infiltrating lymphocytes in cancer: a systematic review with meta-analysis. Br J Cancer 2011;105:93-103.