Original Article

Prognostic significance of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in predicting outcomes for peritoneal carcinomatosis patients treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

ABSTRACT

Background: Laboratory markers of systemic inflammation have demonstrated utility and cost-effectiveness in the prediction of clinical outcome in various malignancies. The aim of the present study is to evaluate the prognostic value of the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in peritoneal carcinomatosis (PC) patients who have undergone cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in a single institution.

Methods: Data were prospectively collected from 164 consecutive patients who underwent CRS-HIPEC procedures between 2001 and 2014, where preoperative NLR and PLR were obtained. The primary endpoints in our study were overall survival (OS) and disease-free survival (DFS). DFS and OS were analyzed using the Kaplan–Meier method. The log-rank test was used to determine if there was a difference in survival between different groups of patients. Univariate and multivariate analyses were performed using the Cox proportional hazards model.

Results: A total of 144 patients underwent 152 CRS-HIPEC procedures, of which 113 females (74.3%) and 31 males (25.6%) with a median age of 51.5 (range 14–74) were included. Neither NLR nor PLR was associated with DFS on univariate analysis. On the exclusion of Peritoneal carcinomatosis index, PLR was significantly associated with DFS, and NLR was not associated with OS on univariate or multivariate analysis. PLR was associated with OS as a continuous or categorical variable with a cutoff of 160 on univariate analysis, but this association disappeared on multivariate analysis.

Conclusion: This study shows that PLR may be more closely associated with recurrence risk and survival of PC patients undergoing CRS-HIPEC than NLR.

Keywords: Cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, peritoneal carcinomatosis, prognostic biomarkers

INTRODUCTION

Peritoneal carcinomatosis (PC) is defined as the presence of cancer cells on the peritoneal surface and can arise from the peritoneum itself or far more commonly from transcoelomic spread from intra-abdominal organs.^[1-3]

Despite attempts at systemic chemotherapy and palliative surgery, patients with PC usually did poorly and were

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given a median survival of 6–12 months.^[4,5] Over the past decade, patients previously forsaken as having an incurable disease are now being given a second lease on life due to the advent of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).^[6]

Currently, the strongest indications for CRS and HIPEC are for (1) PC secondary to colorectal carcinoma, (2) PC secondary to ovarian carcinoma, and (3) pseudomyxoma peritonei secondary to appendiceal mucinous neoplasms.^[6]

A high Peritoneal carcinomatosis index (PCI) and low completeness of cytoreduction (CC) score, together with positive lymph node status, and histopathological type have been found to correlate with poorer prognosis in patients with PC undergoing CRS-HIPEC for mainly colorectal and appendiceal cancers.^[7–9] Similar conclusions with regard to tumor burden before and after CRS have also been drawn in patients with ovarian and primary peritoneal carcinomatosis.^[10,11] However, these prognostic factors rely on intra- and post-operative findings. This means a significant number of patients who are ultimately found to have a poor prognosis with little or no improvement to their disease-free survival (DFS) and overall survival (OS) may undergo the needless morbidity of a CRS-HIPEC.

Recently, there has been interest in using simple serum investigations and their derivatives as biomarkers to be utilized as surrogates for inflammation and hence tumor burden in patients with malignancies. Two such derivatives from a complete blood count (CBC) are neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), have been extensively studied in multiple solid malignancies, and found to correlate with a poorer prognosis in meta-analyses.^[12–14] The prognostic role of NLR has been previously studied in patients with appendiceal PC undergoing CRS-HIPEC,^[15] but data are lacking with regard to its prognostic relevance for the other types of PC commonly treated with CRS-HIPEC. In addition, little data exist for the prognostic significance of PLR for patients with PC undergoing CRS-HIPEC.

The aim of this study was thus to study the prognostic relevance of preoperative NLR and PLR for patients with PC undergoing potentially curative treatment with CRS-HIPEC, in a large tertiary institution in Asia.

METHODS

The data for this study were collected from a prospectively maintained database of all patients undergoing CRS-HIPEC in the National Cancer Centre Singapore.

CBCs taken 24–72 h preoperatively before each case of CRS-HIPEC were used to calculate the ratios needed.

DFS was calculated for each CRS-HIPEC procedure as time from CRS-HIPEC to disease relapse or death from all causes. OS was calculated for each patient as time from first CRS-HIPEC to death from all causes. Disease recurrence or death was recorded as an event.

DFS and OS were analyzed using the Kaplan–Meier method. The log-rank test was used to determine if there was a difference in survival between different groups of patients. Univariable and multivariable analyses were performed using the Cox proportional hazards model. Age, PCI, NLR, and PLR were modeled both as continuous variables (assuming linearity) and categorical variables. The concordance index was used to evaluate the prognostic ability of each of the multivariable models.

The association between variables was assessed using Spearman's correlation (if both variables were continuous) or the Mann–Whitney U test (if one variable was categorical).

A 2-sided $P < 0.05$ was considered statistically significant. All analyses were performed in Stata (Version 12.1, StataCorp, Texas, USA).

This study was approved by the Institutional Review Board.

RESULTS

A total of 164 cases of CRS and HIPEC procedures were performed at the National Cancer Centre, Singapore, between January 1, 2001, and December 31, 2014. One case did not have CRS done, eight cases did not have HIPEC done, and three cases did not have operation details available. After excluding these 12 cases, the analysis was performed on 152 cases of CRS-HIPEC procedures. These 152 cases were from 144 patients; eight patients had two CRS-HIPEC procedures.

The median age of patients was 51.5 (range 14–74). A large proportion of the cases were female (113 cases, 74.3%). Colorectal (53 cases, 34.9%) and ovarian (52 cases, 34.2%) tumors were the most common, followed by appendiceal (31 cases, 20.4%) tumors.

Table 1 summarizes the demographic and baseline characteristics of the cases included in the analyses.

The median follow-up time was 26.5 months (0.36–136.5 months).

Disease-free survival

Univariate analysis

Neither NLR nor PLR was associated with DFS on univariate analysis. Primary tumor type and PCI were the two nonblood parameters in univariate analysis to be most significantly associated with DFS.

Appendiceal tumors (median DFS 25.2 months) and mesothelioma (median DFS 22.0 months) had the best DFS among the tumor types. Ovarian/primary peritoneal tumors had a median DFS of 17.9 months, and colorectal tumors had a median DFS of 9.4 months ($P = 0.012$).

When analyzed as a continuous variable, the PCI was found to be significantly associated with DFS ($P = 0.009$) with a hazard ratio of 1.03 (range 1.01–1.05). Using a cutoff of ≤ 15 versus > 15 , PCI was also significantly associated with DFS. Cases with a PCI ≤ 15 had a median DFS of 18.6 months versus 12.4 months for PCI > 15 ($P = 0.037$). The hazard ratio for PCI > 15 was 1.52 (1.02–2.27) with $P = 0.042$ on univariate analysis.

Multivariate analysis

Based on the univariate analysis that showed that tumor type and PCI were associated with DFS, these parameters were included in the subsequent multivariate analyses. After adjustments for primary tumor type and PCI, neither NLR nor PLR was shown to be significantly associated with DFS on multivariate analysis. These are presented in Table 2.

On attempts to find a significant correlation between NLR or PLR with DFS after exclusion of either primary tumor type or PCI in the multivariate analysis, only PLR became significantly associated with DFS when PCI was excluded, with a hazard ratio 1.02 (1.00–1.03), $P = 0.049$. However, PCI still showed a higher concordance index than PLR (0.672 vs. 0.616). This is represented in Table 3.

Overall survival

Univariate analysis

Primary tumor type was significantly associated with OS. On univariate analysis with the Cox model, hazard ratios for appendiceal, ovarian/primary peritoneal, ovarian, and colorectal tumors were 0.31 (0.12–0.78), 0.50 (0.15–1.68), 0.75 (0.41–1.36), and 1, respectively ($P = 0.050$).

On univariate analysis, a higher PLR was associated with a decrease in OS when considered as a continuous variable for a scaled increase of 10 units, with a hazard ratio of 1.03 (1.02–1.05), $P = 0.002$. The association remained when PLR was analyzed with a cutoff of 160. Cases with PLR ≤ 160

Table 1: Summary of demographics and baseline characteristics (N=152 CRS-HIPEC procedures)

Variable	Frequency (%) or Median (range)
Number of CRS-HIPEC procedures	152 (100%)
Number of 1 st procedures	144 (94.7%)
Number of 2 nd procedures	8 (5.3%)
Age at CRS-HIPEC (years)	51.5 (14–74)
≤ 50	69 (45.4%)
> 50	83 (54.6%)
Gender	
Female	113 (74.3%)
Male	39 (25.7%)
Primary tumour	
Appendix	31 (20.4%)
Colorectal	53 (34.9%)
Mesothelioma	12 (7.9%)
Ovarian	52 (34.2%)
Primary peritoneal	4 (2.6%)
PCI	13 (0–39)
≤ 15	96 (63.2)
> 15	54 (35.5)
Missing	2 (1.3)
CC score	
0	129 (84.9)
1	18 (11.8)
2	3 (2.0)
Missing	2 (1.3)
Pre-operative WBC count ($\times 10^9/L$)	6.60 (2.93–16.86)
Pre-operative percent neutrophils (%)	62.4 (31.0–91.4)
Pre-operative neutrophil count ($\times 10^9/L$)	4.19 (1.70–14.50)
Pre-operative percent lymphocytes (%)	26.2 (3.4–48.0)
Pre-operative lymphocyte count ($\times 10^9/L$)	1.73 (0.35–7.96)
Pre-operative platelet count ($\times 10^9/L$)	267 (95–887)
Neutrophil-lymphocyte ratio	2.42 (0.65–26.88)
≤ 2.5	78 (51.3%)
> 2.5	74 (48.7%)
≤ 5	134 (88.2%)
> 5	18 (11.8%)
Platelet-lymphocyte ratio	154.4 (38.6–1073.7)
≤ 160	81 (53.3%)
> 160	71 (46.7%)

had improved median OS compared to cases with PLR > 160 (106.2 vs. 36.6 months, $P = 0.031$). Cases with PLR > 160 had a hazard ratio of 1.81 (1.05–3.14), $P = 0.033$.

No association could be found between NLR and OS.

PCI also correlated with OS whether it was analyzed as a continuous variable or with a cutoff of 15. As a continuous variable, the hazard ratio for PCI was 1.05 (1.01–1.08), with $P = 0.007$. A PCI of > 15 had a hazard ratio of 1.93 (1.11–3.36) as compared to a PCI of ≤ 15 , with $P = 0.021$.

Table 2: Multivariable analysis of disease-free survival (prognostic value of NLR and PLR after adjusting for primary tumour and PCI)

	Multivariable model 1 (Primary tumour, PCI, NLR)		Multivariable model 2 (Primary tumour, PCI, PLR)	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Primary tumour		<0.001		<0.001
Appendix	0.22 (0.11-0.42)		0.22 (0.12-0.43)	
Colorectal	1		1	
Mesothelioma	0.30 (0.13-0.69)		0.31 (0.13-0.70)	
Ovarian/Primary peritoneal	0.52 (0.33-0.83)		0.51 (0.32-0.80)	
PCI	1.07 (1.04-1.09)	<0.001	1.06 (1.03-1.09)	<0.001
Neutrophil-lymphocyte ratio	0.99 (0.94-1.05)	0.733	Not included	
Platelet-lymphocyte ratio (scaled by 10)	Not included		1.00 (0.99-1.02)	0.593
Concordance index	0.674		0.673	

PCI, NLR and PLR were modelled as continuous variables

Table 3: Multivariable analysis of disease-free survival (comparison of PCI and PLR as prognostic variables)

	Multivariable model 3 (Primary tumour, PCI)		Multivariable model 4 (Primary tumour, PLR)	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Primary tumour		<0.001		0.010
Appendix	0.22 (0.11-0.42)		0.42 (0.24-0.74)	
Colorectal	1		1	
Mesothelioma	0.30 (0.13-0.69)		0.44 (0.20-0.99)	
Ovarian/Primary peritoneal	0.51 (0.32-0.81)		0.62 (0.40-0.97)	
PCI	1.06 (1.04-1.09)	<0.001	Not included	
Platelet-lymphocyte ratio (scaled by 10)	Not included		1.02 (1.00-1.03)	0.049
Concordance index	0.672		0.616	

PCI and PLR were modelled as continuous variables

Table 4: Multivariable analysis of overall survival (prognostic value of NLR and PLR after adjusting for primary tumour, PCI and CC score)

	Multivariable model 1 (Primary tumour, PCI, CC, NLR)		Multivariable model 2 (Primary tumour, PCI, CC, PLR)	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Primary tumour		<0.001		<0.001
Appendix	0.08 (0.03-0.25)		0.10 (0.03-0.31)	
Colorectal	1		1	
Mesothelioma	0.21 (0.06-0.78)		0.24 (0.06-0.90)	
Ovarian/Primary peritoneal	0.60 (0.32-1.12)		0.63 (0.34-1.17)	
PCI	1.07 (1.03-1.12)	<0.001	1.07 (1.02-1.11)	0.002
CC score		0.005		0.017
0	1		1	
1/2	3.78 (1.58-9.07)		3.19 (1.28-7.93)	
Neutrophil-lymphocyte ratio	1.00 (0.93-1.07)	0.943	Not included	
Platelet-lymphocyte ratio (scaled by 10)	Not included		1.01 (1.00-1.03)	0.168
Concordance index	0.725		0.733	

PCI, NLR and PLR were modelled as continuous variables

Cases with CC = 0 had a better median OS than cases with CC = 1/2 (99.9 vs. 28.5 months, $P = 0.011$). The hazard ratio of having a CC = 1/2 was 2.34 (1.20–4.58), with $P = 0.022$.

Multivariate analysis

Primary tumor, PCI, and CC score were significantly associated with OS on univariate analysis; these factors were adjusted for in multivariate models looking at how NLR and PLR affected

OS. Both NLR and PLR were not significantly associated with OS after accounting for the other variables in the model. Primary tumor, PCI, and CC score remained significant in both NLR and PLR models. These are shown in Table 4.

When PCI and CC score were excluded from the multivariate analysis, PLR as a continuous variable became significant for OS, with a hazard ratio of 1.03 (1.02–1.05), $P = 0.001$. However, similar to the multivariate analysis for DFS, PCI,

Table 5: Multivariable analysis of overall survival (comparison of PCI/CC and PLR as prognostic variables)

	Multivariable model 3 (Primary tumour, PCI, CC)		Multivariable model 4 (Primary tumour, PLR)	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Primary tumour		<0.001		0.041
Appendix	0.08 (0.03-0.25)		0.30 (0.12-0.75)	
Colorectal	1		1	
Mesothelioma	0.21 (0.06-0.78)		0.50 (0.15-1.69)	
Ovarian/Primary peritoneal	0.60 (0.32-1.12)		0.73 (0.40-1.34)	
PCI	1.07 (1.03-1.12)	<0.001	Not included	
CC score		0.005	Not included	
0	1			
1/2	3.77 (1.58-9.00)			
Platelet-lymphocyte ratio (scaled by 10)	Not included		1.03 (1.02-1.05)	0.001
Concordance index	0.725		0.651	

PCI and PLR were modelled as continuous variables

and CC score were superior to PLR in terms of prognostic ability (higher concordance index). Table 5 illustrates these findings.

DISCUSSION

Currently, the mechanisms behind the association of high NLR and PLR and worse outcomes among patients with cancer remain incompletely understood. Neutrophilia is associated with inflammation and is known to inhibit the immunological activity of natural killer cells, activated T-cells, and lymphocytes.^[16,17] Tumor progression has been linked to the production of chemokines and inflammatory cytokines by the tumor cells and host leukocytes and platelets.^[18] Indeed, an amplified systemic inflammatory response has been linked to elevated serum levels of multiple cytokines and tumor growth factors that may drive tumor growth.^[19] These include factors such as elastases, vascular endothelial growth factor, hepatocyte growth factor, matrix metalloproteinase, interleukin 8 (IL-8), and IL-6.^[12] IL-6, in particular, has been shown to stimulate thrombocytosis through the production of thrombopoietin in patients with malignancy, and neutrophil recruitment, and is associated with a worse prognosis.^[20,21] Interestingly, IL-6 has also been implicated in the increased synthesis of acute phase proteins (including C-reactive protein) and in the development of hypoalbuminemia, the two biochemical markers used in the Glasgow Prognostic Score.^[22] The importance of tumor-infiltrating lymphocytes was emphasized in a systemic review, which correlated their presence with better response and prognosis in patients with cancer.^[23] Thus, a higher NLR and PLR reflect partly an augmented inflammatory systemic response in a patient, which provides a stimulatory milieu for malignant cells to flourish, and in part a decreased host immune response against tumor cells.

We found that NLR both as a continuous variable and as a categorical variable with cutoff values of 2.5 or 5.0 was not significantly associated with either DFS or OS, in contrast to prior studies performed by other groups. Templeton *et al.* performed a meta-analysis of 100 studies involving more than 40,000 patients regarding the prognostic impact of elevated NLR in solid tumors.^[12] The median cutoff for NLR was 4 (range = 1.9–7.2), with the decision for cutoff values remaining ill-defined in a majority of studies. In this meta-analysis, the hazard ratio for NLR values greater than the cutoff was 1.81 (95% confidence interval = 1.67–1.97; $P < 0.001$), an effect that was observed across all disease subgroups, sites, and stages.

We chose an initial NLR cutoff value of five based on a study of 195 patients who underwent CRS-HIPEC for appendiceal peritoneal carcinomatosis, in which worse OS and progression-free survival were significantly associated with an NLR above a cutoff value of five.^[12] We decided to perform analyses of NLR with half the initial cutoff value (2.5) and as a continuous variable to uncover associations, which may have been inadvertently missed at a cutoff of five. The negative finding of our study should not come as a surprise, as publication bias against negative studies is likely to be prevalent based on the meta-analysis performed by Templeton.

PLR, on the other hand, was found to have a better prognostication value. Another meta-analysis by Templeton *et al.* on the prognostic impact of PLR found an association of high PLR with worse OS in solid tumors.^[13] This study looked at twenty studies involving more than 12,000 patients and found that the size of effect of PLR on OS was greater for metastatic disease than for early-stage disease. Twelve of the twenty studies included had dichotomous risk groups with a PLR cutoff value ranging between 150 and 300, similar to the value of 160 used in our study.

In univariate analysis, PLR was not significantly associated with DFS. However, on multivariable analysis after exclusion of the effects of PCI, a very slight association was seen with DFS (HR 1.02, range = 1.00–1.03; $P = 0.049$). The association of PLR against OS was much clearer. However, this association with OS disappeared when other significant factors (primary tumor, PCI, CC score) in the univariate analysis were adjusted for in multivariate models. This phenomenon can be attributed to the correlation of PLR with elevated PCI and CC score. This was confirmed when the association between PLR and OS again became significant when PCI and CC score were excluded from the multivariate analysis model (hazard ratio 1.03, range 1.03–1.05; $P = 0.001$). The likely mechanism of this relationship is that patients with a higher PCI and CC score have an increased tumor burden with lymphocytic suppression and a reactionary thrombocytosis.^[16-18] The reliability of this association is augmented by the conclusion of two prior meta-analyses that found no evidence of publication evidence.^[13,14]

A higher PCI was associated with a worse DFS on univariate analysis, and this association held firm even on multivariate analysis. A higher PCI and CC score were both found to be significantly associated with a negative impact on OS on univariate analysis, an effect that was persistent even on multivariate analysis. This is in line with findings from Sugarbaker's group when they established that PCI and CC score were independent prognostic factors in patients undergoing CRS-HIPEC for colorectal and appendiceal PC.^[9] PCI is associated with an increased risk of having a higher CC score and reflects the technical limits of the surgical team when faced with higher tumor burden. Although PLR was found to be associated with CC score, NLR was not, and this discordance suggests that the link between tumor burden and inflammatory markers is multifaceted and requires further investigations at the molecular level.

A few shortcomings of this study are apparent. Median follow-up time was just over 2 years (26.5 months), which may not allow for significant differences in prognosis to be appreciated. This study also suffered from a relatively small study size of 144 patients undergoing 152 CRS-HIPEC procedures. In addition, this population was heterogeneously in terms of primary tumor type that would have complicated and/or diluted the true impact of NLR/PLR on DFS and OS. Finally, variables such as number of prior surgical interventions, chemotherapy treatment, and response pre- and post-operatively; type and duration of HIPEC were not accounted for in our analyses.

Limitations of using blood-based inflammatory markers are that they are nonspecific and can be important prognostic

factors in nonmalignant conditions as well.^[24,25] Even though a proportion of patients would have had chemotherapy before their CRS-HIPEC procedure, a sufficient time interval would have passed before they were fit so that their cell counts could be expected to have stabilized. However, the possibility of concurrent inflammatory conditions confounding the effect of blood-based biomarkers cannot be fully excluded.

CONCLUSION

NLR and PLR have emerged recently as possible simple biomarkers for clinicians to prognosticate patients with malignancy, and this concept has similarly been applied to patients undergoing CRS-HIPEC. In our study population, PLR appears to prognosticate better than NLR, but this association may have more to do with PLR's relationship with proven prognostic markers such as PCI and CC score. The ultimate aim of research in this area is to establish a cheap, readily reproducible, and reliable biochemical test that will help clinicians prognosticate patients undergoing CRS-HIPEC for advanced peritoneal malignancies.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sugarbaker PH, Acherman YI, Gonzalez-Moreno S, Ortega-Perez G, Stuart OA, Marchettini P, *et al.* Diagnosis and treatment of peritoneal mesothelioma: The Washington Cancer Institute experience. *Semin Oncol* 2002;29:51-61.
2. Feldman AL, Libutti SK, Pingpank JF, Bartlett DL, Beresnev TH, *et al.* Analysis of factors associated with outcomes in patients with malignant peritoneal mesothelioma undergoing surgical debulking and intraperitoneal chemotherapy. *J Clin Oncol* 2003;21:4560-7.
3. Ceelen WP, Hesse U, de Hemptinne B, Pattyn P. Hyperthermic intraperitoneal chemoperfusion in the treatment of locally advanced intra-abdominal cancer. *Br J Surg* 2000;87:1006-15.
4. Sadeghi B, Arvieux C, Glehen O, Beaujard AC, Rivoire M, Baulieux J, *et al.* Peritoneal carcinomatosis from non-gynecologic malignancies: Results of the EVOCAPE 1 multicentric prospective study. *Cancer* 2000;88:358-63.
5. Verwaal VJ, van Ruth S, de Bree E, van Sloothen GW, van Tinteren H, Boot H, *et al.* Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. *J Clin Oncol* 2003;21:3737-43.
6. Sugarbaker PH. Peritonectomy procedures. *Ann Surg* 1995;221:29-42.
7. Jimenez W, Sardi A, Nieroda C, Sittig M, Milovanov V, Nunez M, *et al.* Predictive and prognostic survival factors in peritoneal carcinomatosis from appendiceal cancer after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. *Ann Surg Oncol* 2014;21:4218-25.
8. Yonemura Y, Canbay E, Ishibashi H. Prognostic factors of peritoneal metastases from colorectal cancer following cytoreductive

- surgery and perioperative chemotherapy. *ScientificWorldJournal* 2013;2013:978394.
9. Sugarbaker PH, Jablonski KA. Prognostic features of 51 colorectal and 130 appendiceal cancer patients with peritoneal carcinomatosis treated by cytoreductive surgery and intraperitoneal chemotherapy. *Ann Surg* 1995;221:124-32.
 10. Cotte E, Glehen O, Mohamed F, Lamy F, Falandry C, Golfier F, *et al.* Cytoreductive surgery and intraperitoneal chemo-hyperthermia for chemo-resistant and recurrent advanced epithelial ovarian cancer: Prospective study of 81 patients. *World J Surg* 2007;31:1813-20.
 11. Eltabbakh GH, Werness BA, Piver S, Blumenson LE. Prognostic factors in extraovarian primary peritoneal carcinoma. *Gynecol Oncol* 1998;71:230-9.
 12. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, *et al.* Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: A systematic review and meta-analysis. *J Natl Cancer Inst* 2014;106:dju124.
 13. Templeton AJ, Ace O, McNamara MG, Al-Mubarak M, Vera-Badillo FE, Hermanns T, *et al.* Prognostic role of platelet to lymphocyte ratio in solid tumors: A systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2014;23:1204-12.
 14. Zhou X, Du Y, Huang Z, Xu J, Qiu T, Wang J, *et al.* Prognostic value of PLR in various cancers: A meta-analysis. *PLoS One* 2014;9:e101119.
 15. Kusamura S, Baratti D, Hutani I, Gavazzi C, Morelli D, Iusco DR, *et al.* The role of baseline inflammatory-based scores and serum tumor markers to risk stratify pseudomyxoma peritonei patients treated with cytoreduction (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). *Eur J Surg Oncol* 2015;41:1097-105.
 16. Petrie HT, Klassen LW, Kay HD. Inhibition of human cytotoxic T lymphocyte activity *in vitro* by autologous peripheral blood granulocytes. *J Immunol* 1985;134:230-4.
 17. el-Hag A, Clark RA. Immunosuppression by activated human neutrophils. Dependence on the myeloperoxidase system. *J Immunol* 1987;139:2406-13.
 18. Balkwill F, Mantovani A. Inflammation and cancer: Back to Virchow? *Lancet* 2001;357:539-45.
 19. Kantola T, Klintrup K, Väyrynen JP, Vornanen J, Bloigu R, Karhu T, *et al.* Stage-dependent alterations of the serum cytokine pattern in colorectal carcinoma. *Br J Cancer* 2012;107:1729-36.
 20. Klinger MH, Jelkmann W. Role of blood platelets in infection and inflammation. *J Interferon Cytokine Res* 2002;22:913-22.
 21. Lippitz BE. Cytokine patterns in patients with cancer: A systematic review. *Lancet Oncol* 2013;14:e218-28.
 22. Ohsugi Y. Recent advances in immunopathophysiology of interleukin-6: An innovative therapeutic drug, tocilizumab (recombinant humanized anti-human interleukin-6 receptor antibody), unveils the mysterious etiology of immune-mediated inflammatory diseases. *Biol Pharm Bull* 2007;30:2001-6.
 23. 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.
 24. Azab B, Jaglall N, Atallah JP, Lamet A, Raja-Surya V, Farah B, *et al.* Neutrophil-lymphocyte ratio as a predictor of adverse outcomes of acute pancreatitis. *Pancreatol* 2011;11:445-52.
 25. Park JJ, Jang HJ, Oh IY, Yoon CH, Suh JW, Cho YS, *et al.* Prognostic value of neutrophil to lymphocyte ratio in patients presenting with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Am J Cardiol* 2013;111:636-42.