Observational Study

Medicine®

OPEN

Elevated neutrophil to lymphocyte ratio predicts mortality in medical inpatients with multiple chronic conditions

Vivian Isaac (MPhil)[a], Chia-Yi Wu (PhD)[b,*], Chun-Ta Huang (MD)[c], Bernhard T. Baune (MD, PhD)[d], Chia-Lin Tseng (MD)[c], Craig S. McLachlan (PhD)[a]

Abstract

Neutrophil to lymphocyte ratio (NLR) is an easy measurable laboratory marker used to evaluate systemic inflammation. Elevated NLR is associated with poor survival and increased morbidity in cancer and cardiovascular disease. However, the usefulness of NLR to predict morbidity and mortality in a hospital setting for patients with multiple chronic conditions has not been previously examined. In this study, we investigate the association between NLR and mortality in multimorbid medical inpatients. Two hundred thirty medical in-patients with chronic conditions were selected from a single academic medical center in Taiwan. Retrospective NLRs were calculated from routine full blood counts previously obtained during the initial hospital admission and at the time of discharge. Self-rated health (using a single-item question), medical disorders, depressive symptoms, and medical service utilization over a 1-year period were included in the analyses. Mortality outcomes were ascertained by reviewing electronic medical records and follow-up. The mortality rate at 2-year follow-up was 23%. Depression (odds ratio [OR] 1.9 [95% CI 1.0–3.7]), poor self-rated health (OR 2.1 [95% CI 1.1–3.9]), being hospitalized 2 or more times in the previous year (OR 2.3 [95% CI 1.2–4.6]), metastatic cancer (OR 4.7 [95% CI 2.3–9.7]), and chronic liver disease (OR 4.3 [95% CI 1.5–12.1]) were associated with 2-year mortality. The median (interquartile range) NLR at admission and discharge were 4.47 (2.4–8.7) and 3.65 (2.1–6.5), respectively. Two-year mortality rates were higher in patients with an elevated NLR at admission (NLR $<3=15.5\%$, NLR $>3=27.6\%$) and discharge (NLR $<3=14.7\%$, NLR $>3=29.1\%$). Multivariate logistic regression demonstrated that an elevated NLR >3.0 at admission (OR 2.3 [95% CI 1.0–5.2]) and discharge (OR 2.3 [95% CI 1.1–5.0]) were associated with mortality independent of baseline age, sex, education, metastatic cancer, liver disease, depression, and previous hospitalization. Increased NLR is associated with mortality among medical inpatients with multiple chronic conditions. NLR may provide added value to predict both risk of mortality for the inpatients with chronic conditions, in addition to allowing predictions of likely hospital service needs such as re-admissions that are associated with long-term mortality.

Abbreviations: CCI = Charlson comorbidity index, LTE-Q = Life-threatening Event Questionnaire, NLR = neutrophil to lymphocyte ratio, PHQ-9 = The Patient Health Questionnaire-9, SRH = self-rated health.

Keywords: chronic conditions, medical service use, mortality, neutrophil-lymphocyte ratio

1. Introduction

Serious chronic disease often requires patients to be hospitalized. Outcomes in chronic disease leading to death are often associated with poor self-rated health and variable increases in hospital transitions and differential health care costs. For this reason, there is interest in finding and using novel biomarkers that may better predict or identify in-hospital patients that are likely to use future hospital services more frequently.[1,2]

Death has been considered as a surrogate outcome measure for modeling end of life chronic disease hospital utilization.[3] However, death while investigatory may not always be useful, particularly if proceeding and predictive factors have not been captured.[3] Approximately, a quarter of lifetime health care are consumed in the last year of life yet it is still very difficult to model associated increased health care utilization in at-risk patients.[3] Death may be associated with any number of preceding factors such as poorer self-rated health, depression, and increased hospital utilization over a defined period of time. Chronic inflammation is a well-accepted biomarker that intersects and influences both psychological well-being and health-seeking behaviors.[4,5] The role of inflammation has not been well characterized as a predictor for all-cause mortality during longitudinal tracking of mixed cohorts of chronic disease patients who have been postdischarged from hospital.

Simple measures to assess inflammation are available such as the neutrophil to lymphocyte ratio (NLR), a white cell count differential routinely reported on full blood counts. In addition, because the NLR is derived from full blood counts, it is amenable

Editor: Shankar Esaki Muthu.

The authors report no conflicts of interest.

[a] Rural Clinical School, University of New South Wales, Sydney, Australia,
[b] School of Nursing, College of Medicine, National Taiwan University,
[c] Department of Traumatology, National Taiwan University Hospital, Taiwan,
[d] Department of Psychiatry, School of Medicine, University of Adelaide, Adelaide, Australia.

[*] Correspondence: Chia-Yi Wu, School of Nursing, College of Medicine National Taiwan University 1, Jen-Ai Road, Section 1, Taipei 100, Taiwan (e-mail: jennycyw@ntu.edu.tw).

Medicine (2016) 95:23(e3832)

Received: 12 October 2015 / Received in final form: 4 May 2016 / Accepted: 10 May 2016

Published online 1 May 2016

http://dx.doi.org/10.1097/MD.0000000000003832

to both prospective and retrospective studies. Elevated NLR is associated with poor survival and increased morbidity in cancer, critical care, and cardiovascular disease.[6–9] However, NLR has not been evaluated with respect to being an independent predictor for mortality when contrasting health service utilization for chronic disease cohorts. Our aims are to determine the usefulness of NLR to predict mortality for patients with multiple chronic conditions in a hospital setting. Secondary aims are to assess if NLR is an independent predictor of mortality when contrasted with self-rated health (SRH), depression, medical service use, and chronic conditions.

2. Methods

2.1. Study context and procedures

This prospective study was conducted in a university-affiliated medical center. Consecutive medical inpatients with various physical chronic illnesses admitted through the emergency department were recruited to the study between November 2012 and 2013 in northern Taiwan. All-cause mortality was recorded after 2 years follow-up. The ethical approval was acquired from the study hospital (reference number: 201112091RIC).

Exclusion criteria included patients with moderate to severe cognitive dysfunction assessed by the Short Portable Mental State Questionnaire adjusted for level of education, for example, at most 3 item errors for those with education years at least 12 was classified as mild cognitive impairment.[10] This is a hypothesis generating substudy of a previous study,[11] and therefore for consistency some methods are repeated and cited where appropriate.

3. Measurements

3.1. Blood sample analyses

Routine blood tests were carried out during the initial hospital admission and discharge. Discharge was defined as treatment accomplishment in the index admission. Leukocyte, neutrophil, lymphocyte, monocyte counts were derived from clinical records. All counts were derived from the same hospital clinical biochemistry department. NLR was calculated as the ratio of neutrophils to lymphocytes, and both obtained from the same blood sample. The cutoffs of NLR values were set at 3 to define different levels of the ratio based on the tertiles of the total scores in the sample. An NLR >3 was shown to have significant prognostic effect in cancer patients.[12,13]

3.2. Chronic medical conditions

The primary admitting diagnosis and secondary chronic conditions were obtained from the patients' electronic medical records.[11] The Charlson comorbidity index [14] was used to assess comorbidities. We recorded each medical illness encompassing cancer and major organ systems including brain, heart, liver, kidney, and the blood system.

3.3. Depressive symptoms

Severity of depressive symptoms assessed using The Patient Health Questionnaire-9 (PHQ-9).[11] The Chinese version of the PHQ-9 is validated and has shown good reliability in hospital and primary care patients in Taiwan.[15]

3.4. Threatening life events

The variable refers to significant life events over the last 12 months that could be classified as stressful or life-threatening using the Life-threatening Event Questionnaire.[11,16]

3.5. Lifetime suicide ideation

Patients' lifetime suicide ideation was assessed as an indicator of suicide risk.[11] Other risk factors of suicide such as *e*xcessive ethanol or drug use, *r*ational thinking loss, poor social support were assessed based on a brief rating scale, the Chinese SAD PERSONS Scale.[17]

3.6. Self-rated health

The participants were asked about their general health conditions via a single question[11]: "In general terms, how would you describe your overall health status: very good, good, fair, poor, or very poor?"

3.7. Medical utilization

The frequency of medical service utilization was recorded as the number of visits to medical out-patient services, emergency services, and hospitalization services in the past 12 months.[11]

3.8. Mortality

The clinical endpoint was all-cause mortality. Mortality ascertained by reviewing hospital electronic medical records or during telephone follow-up.

3.9. Data analysis

Univariate and bivariate analyses were conducted before multivariate analyses. Chi-squared tests and odds ratios (ORs) with their 95% confidence intervals (CIs) were used to assess associations between independent variables and mortality. Multivariate logistic regression was applied to investigate the independent effect of NLR on mortality after adjustment of factors that showed an association with mortality. Separate analyses were conducted for NLR at admission and discharge. The models were adjusted for age, sex, education, metastatic cancer, liver disease, SRH, frequent use of outpatient department in the previous year and hospitalized in the previous year. All statistical analyses were performed using the SPSS v21, and statistical significance was defined at a value of $P<0.05$.

4. Results

The mean (SD) age of our sample was 62.6 (16.1) years and women constituted 46.5%. The baseline demographic factors and blood count values are reported in Table 1. The median (IQR) values of neutrophil, lymphocyte, and NLR were 5.73 (3.3–9.1), 1.12 (0.7–2.3), and 4.47 (2.4–8.7), respectively, at admission. At discharge, the median neutrophil count was 4.71 (2.9–6.9), median lymphocyte count was 1.24 (0.8–1.7), and NLR was 3.65 (2.1–6.5). The mortality rate was 23%, with 53 of 230 patients who died during the 2-year follow-up period.

Table 2 explains the association between various study variables and mortality. Men were at a higher risk of mortality at 2 years (OR 1.9 [95% CI 1.0–3.7]). Presence of depression (OR 1.9 [95% CI 1.0–3.7]) and poor SRH (OR 2.1 [95% CI

Table 1

Characteristics and whole blood count at admission of study participants

Characteristics	
Age, mean ± SD	62.6 ± 16.0
Gender, n (%)	
Female	107 (46.5)
Male	123 (53.5)
Years of education, mean ± SD	9.6 ± 5.8
Marital status, n (%)	
Single	27 (11.7)
Married	142 (61.7)
Divorced/separated	26 (11.3)
Widowed	35 (15.2)
Living alone, n (%)	
No	212 (92.2)
Yes	18 (7.8)
Blood count (admission)	
WBC count (10e9/l), median (IQR)	7.83 (5.2–11.4)
Neutrophil count (10e9/l), median (IQR)	5.73 (3.3–9.1)
Lymphocyte count (10e9/l), median (IQR)	1.12 (0.7–2.3)
NLR, median (IQR)	4.47 (2.4–8.7)
Blood count (discharge)	
WBC count (10e9/l), median (IQR)	6.92 (5.0–11.3)
Neutrophil count (10e9/l), median (IQR)	4.71 (2.9–6.9)
Lymphocyte count (10e9/l), median (IQR)	1.24 (0.8–1.7)
NLR, median (IQR)	3.65 (2.1–6.5)

IQR, interquartile range; NLR, neutrophil to lymphocyte ratio.

1.1–3.9]) were associated mortality at 2 years. Lifetime suicide ideation and life-threatening events in the past year were not associated with mortality at 2 years. A statistically significant association was observed among frequent hospital admissions and mortality (OR 2.3 [95% CI 1.2–4.6]). Among medical conditions, metastatic cancer (OR 4.7 [95% 2.3–9.7]) and chronic liver disease (OR 4.3 [95% CI 1.5–12.1]) were associated with mortality at 2 years. Mortality rates were higher for those with elevated levels of NLR (>3) at admission (OR 2.0 [OR 1.0–4.2]) and discharge (OR 2.4 (95% CI 2.4 (1.2–4.7)). Log-transformed NLR as a continuous variable had a similar association with mortality at admission ($t=-1.9$, $P=0.05$) and discharge ($t=-2.9$, $P=0.004$).

We modeled the association between NLR and mortality in multivariate logistic regression model (Table 3). On separate analyses, patients with an NLR > 3 at admission (OR 2.3 [95% CI 1.0–5.2]) and discharge (OR 2.3 [95%CI 1.1–5.0]) were associated with mortality independent of baseline age, sex, education, metastatic cancer, liver disease, depression, and previous hospitalization.

5. Discussion

Our findings show that NLR carries important prognostic information in chronic non-ICU patients regarding their mortality outcomes. Data were derived from a mixed chronic illness cohort. Disease subgroups had similar stages of chronic disease upon entry into the study. Specifically, we found an NLR > 3 were associated with increased follow-up mortality at 2 years. Male patients, patients with depression, chronic liver disease or metastatic cancer, had a higher mortality rate.

For our study population, we observed a median NLR of 5.73 at the time of hospital admission. This suggests that a significant proportion of patients were ill with high levels of systemic inflammation. These NLR levels are lower than (median NLR 8.9) those observed across a large group of ICU patients. In the ICU study, NLR was measured at the time of admission to ICU. Higher NLR levels were associated with 28-day mortality in unselected critically ill patients.[8] There was no attempt to

Table 2

Factors associated with mortality at 2-year follow-up

	Mortality			
	n	%	OR (95% CI)	*P*
Age, y				
20-40	5	26.3	1.0	0.83
41-60	17	20.2	0.7 (0.2–2.2)	
61-80	22	25.9	0.9 (0.3–3.0)	
>81	9	21.4	0.8 (0.2–2.7)	
Gender				
Female	18	16.8	1.0	
Male	35	28.5	2.0 (1.0–3.7)	0.04
Blood count				
NLR at admission				
≤3.0	13	15.5	1.0	
>3.0	40	27.6	2.0 (1.0–4.2)	0.05
NLR at discharge				
≤3.0	14	14.7	1.0	
>3.0	39	29.1	2.4 (1.2–4.7)	0.01
Hypertension				
No	36	29.0	1.0	0.03
Yes	17	16.0	0.5 (0.2–0.9)	
Diabetes				
No	44	25.3	1.0	
Yes	9	16.1	0.6 (0.6–1.2)	0.20
Liver disease				
No	45	20.9	1.0	
Yes	8	53.3	4.3 (1.5–12.1)	0.004
Kidney disease				
No	45	24.5	1.0	
Yes	8	17.4	0.6 (0.2–1.4)	0.43
Metastatic cancer				
No	33	17.4	1.0	
Yes	20	50.0	4.7 (2.3–9.7)	0.001
Psychosocial status				
Life-threatening event in the past year				
No	30	20.3	1.0	
Yes	23	28.0	1.5 (0.8–2.9)	0.19
Lifetime suicide ideation				
No	39	23.9	1.0	
Yes	14	20.9	0.8 (0.4–1.7)	0.73
Depression (PHQ ≥ 10)				
No	31	19.3	1.0	
Yes	22	31.9	1.9 (1.0–3.7)	0.04
Poor SRH				
No	18	16.4	1.0	
Yes	35	29.2	2.1 (1.1–3.9)	0.02
Frequent use of OPD*				
No	30	19.6	1.0	
Yes	23	29.9	1.7 (0.9–3.2)	0.08
Frequent users of ED				
No	34	20.9	1.0	
Yes	19	28.4	1.5 (0.8–2.8)	0.22
Frequent users of hospitalization services				
No	35	19.4	1.0	
Yes	18	36.0	2.3 (1.2–4.6)	0.02

CI, confidence interval; ED, emergency department; NLR, neutrophil to lymphocyte ratio; OPD, outpatient department; OR, odds ratio; PHQ, Patient Health Questionnaire; SRH, self-rated health.
*Frequent users were defined as those visited or admitted to the outpatient department, emergency department, and hospitalization for >14, 2, and 2 times in the past year of recruitment.

Table 3

Multivariate logistic regression model: NLR, psychological factors, and health service use

	Mortality at 2-year follow-up			
	OR (95% CI)	*P*	OR (95% CI)	*P*
NLR >3.0 baseline	2.3 (1.0–5.2)	0.04		
NLR >3.0 follow-up			2.3 (1.1–5.0)	0.03
Baseline factors				
Age	1.0 (0.7–1.6)	0.67	1.1 (0.7–1.7)	0.57
Gender (male)	3.1 (1.4–6.7)	0.004	2.7 (1.2–5.8)	0.01
Metastatic cancer	5.1 (2.1–11.1)	<0.001	4.9 (2.1–11.5)	<0.001
Chronic liver disease	8.8 (2.6–29.9)	<0.001	9.0 (2.6–30.3)	<0.001
Depression (PHQ ≥ 10)	2.3 (1.0–4.9)	0.03	2.3 (1.0–5.0)	0.03
Poor SRH	0.9 (0.4–2.1)	0.96	1.1 (0.5–2.4)	0.83
Frequent use of OPD in the previous year*	1.0 (0.5–2.5)	0.83	1.1 (0.1–2.6)	0.75
Frequent users of hospitalization services	2.4 (0.9–6.3)	0.07	2.1 (0.8–5.4)	0.11

CI, confidence interval; NLR, neutrophil to lymphocyte ratio; OPD, outpatient department; OR, odds ratio; PHQ, Patient Health Questionnaire; SRH, self-rated health. Model includes age, sex, education, metastatic cancer, liver disease, SRH, frequent use of OPD, Outpatient Department in the previous year and hospitalized in the previous year.

* Frequent users were defined as those visited or admitted to the outpatient department, emergency department, and hospitalization for >14, 2, and 2 times in the past year of recruitment.

stratify patients on the basis of admission characteristics other than sepsis or nonsepsis,[8] we have stratified on the basis of chronic illness in our study. On the other hand, the patients in our study had a median NLR of 3.65 at the time of their discharge in the index hospitalization, suggesting hospital patients were significantly unwell at the time of discharge with underlying systemic inflammation. Patients with an NLR > 3 (arbitrary cutoffs) at both admission and discharge had a greater risk for death later on. In multivariate models, after adjusting for both depression and medical utilization, NLR remained an independent predictor of mortality outcomes.

We found elevated NLR was associated with an increase in mortality for liver and cancer patients but not hemodialysis, diabetes, or hypertension patients. In a previous chronic hemodialysis study, hospitalization was shown to increase in parallel with increases in progressive NLR levels over 5 years of retrospective review.[18] Our period of follow-up for hemodialysis patients was a shorter 2-year period. Both diabetes and hypertension are risk factors for cardiovascular disease that can also promote systemic inflammation. We did not find any interaction of diabetes and hypertension on mortality outcomes (data not shown). In previous studies, NLR's ability to predict renal failure was independent of patient's heart failure and systolic/diastolic blood pressure status. In addition, not all chronic conditions are associated with increased NLR levels. In Asian populations, diabetes and hypertension may be associated with NLR but not asthma or arthritis when adjusting for their interactions in multiple comorbidity models.[19] In other studies, NLR is a strong predictor of 3-month mortality in patients with acute-on-chronic liver failure.[20] An increasing number of studies demonstrate that changes in NLR are associated with poor cancer-specific survival.[21] NLR in precancer surgery has emerged as a strong risk predictor of mortality in patients with a range of cancer subtypes including colorectal, gastric, hepatocellular, pancreatic, and lung cancer.[22,23] Pretreatment NLR is also a strong predictor of longer term 5-year survival outcomes in breast cancer patients.[21] White cell subpopulations can change in numbers as a response to inflammation found within tumor microenvironments[24,25] and/or as a result of psychological stress.[21] It is plausible that increases in white cell populations may be associated with concurrent levels of depression and poor rated self-health. The tumor microenvironment is influenced by both local and systemic inflammation states.[24,25] A cancer diagnosis in many instances leads to significant psychological distress in up to 75% of cancer cases, and the diagnosis of secondary cancer in the liver has been reported to further increase patient distress levels.[21,22] However, when these factors were controlled for, NLR remained a significant prognostic factor for mortality. Reversible changes in the distribution of peripheral blood leukocyte subpopulations in the blood provide an important representation of the state of activation of the immune system under perceived distress.

Self-coping and disease progression play a central role in health seeking.[26] Factors influencing health-seeking behavior may include changes in clinician and patient behavior, and/or changes in severity of underlying disease.[27] In our study, the high median admission NLR levels would indicate a high level of baseline severity for underlying disease in some of the chronic hospitalized patients in our study. Of note, we found that frequency of in-hospital admissions were a predictor of mortality, whereas emergency department admissions were not. This finding may parallel previous studies where planned care alone does not account for the increases in all-cause ED presentations following a cardinal chronic health event.[3] It would appear that higher NLR is a strong predictor for both mortality and subsequent medical utilization. A persistently high NLR at the time of discharge is likely to be a predictor for increased medical utilization and mortality risk.

Acknowledgments

The study was funded by the Ministry of Science and Technology in Taiwan (reference number: NSC 101–2511-S-002 -005). The authors appreciate all the participants of this study and the research assistant who helped collect the data.

References

[1] Ho KM, Lee KY, Dobb GJ, et al. C-reactive protein concentration as a predictor of in-hospital mortality after ICU discharge: a prospective cohort study. Intensive Care Med 2008;34:481–7.

[2] Ranzani OT, Zampieri FG, Forte DN, et al. C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. PloS One 2013;8: e59321.

[3] Whyatt D, Tenneti R, Marsh J, et al. The ratchet effect: dramatic and sustained changes in health care utilization following admission to hospital with chronic disease. Med Care 2014;52:901–8.

[4] Chang C, Zhu H, Shen N, et al. Utility of the combination of serum highly-sensitive C-reactive protein level at discharge and a risk index in predicting readmission for acute exacerbation of COPD. J Bras Pneumol 2014;40:495–03.
[5] Maes M. Depression is an inflammatory disease, but cell-mediated immune activation is the key component of depression. Prog Neuro-psychopharmacol Biol Psychiatry 2011;35:664–75.
[6] Kumar R, Geuna E, Michalarea V, et al. The neutrophil-lymphocyte ratio and its utilisation for the management of cancer patients in early clinical trials. Br J Cancer 2015;112:1157–65.
[7] Paramanathan A, Saxena A, Morris DL. A systematic review and meta-analysis on the impact of pre-operative neutrophil lymphocyte ratio on long term outcomes after curative intent resection of solid tumours. Surg Oncol 2014;23:31–9.
[8] Salciccioli JD, Marshall DC, Pimentel MA, et al. The association between the neutrophil-to-lymphocyte ratio and mortality in critical illness: an observational cohort study. Crit Care 2015;19:13.
[9] Proctor MJ, McMillan DC, Horgan PG, et al. Systemic inflammation predicts all-cause mortality: a glasgow inflammation outcome study. PloS One 2015;10:e0116206.
[10] Wu CY, Su TP, Fang CL, et al. Sleep quality among community-dwelling elderly people and its demographic, mental, and physical correlates, Journal of the Chinese Medical Association. JCMA 2012;75:75–80.
[11] Isaac V, McLachlan CS, Baune BT, et al. Poor self-rated health influences hospital service use in hospitalized inpatients with chronic conditions in Taiwan. Medicine 2015;94:e1477.
[12] Jung MR, Park YK, Jeong O, et al. Elevated preoperative neutrophil to lymphocyte ratio predicts poor survival following resection in late stage gastric cancer. J Surg Oncol 2011;104:504–10.
[13] Lee S, Oh SY, Kim SH, et al. Prognostic significance of neutrophil lymphocyte ratio and platelet lymphocyte ratio in advanced gastric cancer patients treated with FOLFOX chemotherapy. BMC cancer 2013;13:350.
[14] Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
[15] Liu S-I, Yeh Z-T, Huang H-C, et al. Validation of Patient Health Questionnaire for depression screening among primary care patients in Taiwan. Compr Psychiatry 2011;52:96–101.
[16] Brugha TS, Cragg D. The list of threatening experiences: the reliability and validity of a brief life events questionnaire. Acta psychiatrica Scandinavica 1990;82:77–81.
[17] Wu CY, Huang HC, Wu SI, et al. Validation of the Chinese SAD PERSONS Scale to predict repeated self-harm in emergency attendees in Taiwan. BMC Psychiatry 2014;14:44.
[18] Usvyat LA, Kooman JP, van der Sande FM, et al. Dynamics of hospitalizations in hemodialysis patients: results from a large US provider. Nephrology Dialysis Transplantation 2014;29:442–8.
[19] Imtiaz F, Shafique K, Mirza SS, et al. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. Int Arch Med 2012;5:2.
[20] Chen L, Lou Y, Chen Y, et al. Prognostic value of the neutrophil-to-lymphocyte ratio in patients with acute-on-chronic liver failure. Int J Clin Pract 2014;68:1034.
[21] Azab B, Shah N, Radbel J, et al. Pretreatment neutrophil/lymphocyte ratio is superior to platelet/lymphocyte ratio as a predictor of long-term mortality in breast cancer patients. Med Oncol 2013;30:432.
[22] Guthrie GJ, Charles KA, Roxburgh CS, et al. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. Crit Rev Oncol Hematol 2013;88:218–30.
[23] Donskov F. Immunomonitoring and prognostic relevance of neutrophils in clinical trials. Semin Cancer Biol 2013;23:200–7.
[24] Coussens LM, Werb Z. Inflammation and cancer. Nature 2002;420: 860–7.
[25] Colotta F, Allavena P, Sica A, et al. Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability. Carcinogenesis 2009;30:1073–81.
[26] Li CC, Shun SC. Understanding self care coping styles in patients with chronic heart failure: a systematic review. Eur J Cardiovasc Nurs 2016;15:12–9.
[27] Saunders ND, Nichols SD, Antiporda MA, et al. Examination of unplanned 30-day readmissions to a comprehensive cancer hospital. J Oncol Pract 2015;11:e177–81.