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Original Article

Frailty in Older Patients Referred to Oncology, and Impact of Treatment: Use of a Modified 6 Item Score

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ABSTRACT

Aims: Retrospectively audit the outcome of frail older patients referred to a regional medical oncology service in New Zealand and assess the 8 item G8 frailty score.

Methods: For all patients 75 years and older assigned a first assessment at the medical oncology service over 12 months, data on diagnosis and health status was collected, and the G8 score determined.

Results: 305 of the 350 given an appointment attended, 52% were male, 53% had metastatic disease, 29% had colorectal cancer. If aged 84+ years, 50% deteriorated or died within 6 months. Age, cancer diagnosis, stage, and higher neutrophil/lymphocyte ratio were associated with poor outcome at 6 months; use of chemotherapy, endocrine therapy, radiation and surgery with better outcome. Data allowed use of 6 items from the G8 score; with 55% classified frail or vulnerable on G6 score. At 6 months 62.7% deemed frail had deteriorated or died, compared with 22.9% of those not frail.

Conclusion: In patients with a new cancer diagnosis aged 75 years and older, outcome at 6 months was associated with age, cancer type, stage, treatment and G6 score. The G6 frailty score used age, weight and height (BMI), loss of appetite, decreased mobility, self-declared health status and medication use, and should be tested prospectively.

The proportion of older people in the population is steadily increasing, with those older than 65 years expected to double to 25%, by 2043 compared with 2016 [1]. The incidence of most cancers increases with age, and in New Zealand 30% of all new cancer diagnoses in 2013 were in people aged 75 and older [2]. Increasing numbers of older people are referred to Oncology Services for treatment of cancer. Patients often ask whether proposed treatments might take away their independence. While the stage of the cancer and its biology are important in predicting outcome, patient factors influence their ability to withstand treatments and resilience to side effects. We wished to find a simple tool to help predict the likelihood of being well at 3 and 6 months and hence the likely benefit of anti-cancer therapy, or whether best supportive care alone would be the appropriate choice.

There are a number of definitions or tools for "frailty" for non-Oncology populations, including the frailty phenotype described by Fried [3, 4]. Gradually, more relevant scores are being developed for older people with cancer, for example for predicting adverse effects from chemotherapy, CRASH (Chemotherapy Risk Assessment Scale for High-Age Patients) and CARG (Cancer and Aging Research Group) scores [5, 6]. The International Society of Geriatric Oncology (SIOG) developed a geriatric assessment tool known as "SIOG1" or "G8" for use with men with prostate cancer, as it was felt that age alone was

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insufficient to determine if treatment was suitable for elderly patients [7, 8]. This has been evaluated by Bellera [9]. Patients are sorted into not frail, who have a score of 15-17, who are not further evaluated, and those with scores of 14 or lower are "frail" or "vulnerable", and are further assessed for comorbidities and dependence status (activities of daily living, ADLs, and independent ADLs, (iADLs) [8, 9]. Vulnerable people who respond to appropriate interventions can be considered for standard therapies, while those who do not improve are regarded as frail, and treatment is adapted [8]. The contributing items can largely be derived from clinical records and comorbidity is determined by Charlson index [10]. When the SIOG1 score was compared with 3 other classifications, it best predicted death at one year, while all four predicted Hospital admission within 6 months [11].

Neutrophil/lymphocyte (N/L) ratio in peripheral blood has been proposed as a marker for prognosis, with higher neutrophil levels associated with worse prognosis for example in colorectal cancer, and non-small cell lung cancer [12-14]. Similar associations have been shown for many cancers, especially if levels exceed 4 [15, 16]. However, N/L ratio is higher at older age in normal populations [17]. We therefore also explored the possible value of neutrophil /lymphocyte ratio, since these values are almost universally recorded. Our aim was to audit the 3- and 6-month outcome of an unselected consecutive one-year cohort of patients aged 75 years and older referred to a regional medical oncology service in New Zealand, and to assess the SIOG1 (G8 score) retrospectively. In addition, the prognostic value of neutrophil/lymphocyte ratio was explored.

Methods

A retrospective audit was conducted on all people 75 years and older, with a referral to the medical oncology service at Christchurch Hospital between 1 June 2016 and 1 June 2017. Patients were identified through Mosaiq (the electronic oncology database at Canterbury Regional Cancer and Haematology Service, Christchurch Hospital), with all those assigned a First Specialist Assessment (FSA) appointment included. These were new referrals, who had not been previously seen in the service, as well as re-referrals of patients who had either a new cancer or recurrence having been previously seen but discharged. Health Connect South (the South Island electronic medical records database) and Mosaiq were searched by one author (CW) for, clinical data collected at FSA, including medical diagnoses, current medications, cancer diagnosis and stage, weight, height, domicile, mobility, support, report of weight loss, and on follow-up, cancer treatment, health status and outcome at 3 and 6 months. Neutrophil and lymphocyte count were taken from blood count within 30 days of FSA.

Table 1: Items in G8 score, SIOG 1, as described by Droz et al. 2010, 2014, with scores [7, 8].

Item	Score 0	Score 1	Score 2	Score 3	
Age	>85yrs	80-85yrs	<80yrs		
Weight loss	>3kg	does not know	1-2 Kg weight loss	3, no weight loss	
BMI, Kg/m^2	<19	19-20.9	21-22.9	3, >22.9	
Nutrition, food intake	severe decrease intake	moderate reduction intake	normal intake		Omit G6
Mobility	chair/bed bound	mobile in home	goes out		
Drugs >3/day	<4 per day	>3/day			
Neuropsychological problems	severe dementia or depression	mild dementia	no problems		Omit G6, G7
Self-rating	not as good as others	as good as others	better than others		

The G8 score which is shown in (Table 1) takes into account age, weight loss, body mass index (BMI), nutrition as food intake, mobility, more than 3 drugs daily at diagnosis, neuropsychological problems, and self-rating against others [7-9]. At FSA BMI was determined, and analysed using the G8 score cut-offs, called G8 BMI, and also using the WHO criteria [8-12]. Patients were deemed either frail (included vulnerable), G8 score 14 or less, or not frail, score greater than 14. Self-rating against peers at diagnosis was inferred by one observer from the records and is subjective. Since information for two items (nutrition and neuropsychological) of the G8 score was missing for many patients, the G6 (and G7) scores were also determined, with a G6 score of 10 or less for frail or vulnerable. (This was based on the possible maximum score of 2 for each of the two omitted criteria.) Health status was assessed at 3 and 6 months from the cancer diagnosis which had prompted the FSA. For the majority of the patients formal restaging as would occur in a clinical trial e.g. using RECIST criteria, was not performed as part of their standard care. Therefore, a rating score adapted for this audit from the Palliative Care Phase was used and patient status interpreted from clinical follow up letters and rated "improved", "stable", "deteriorated" or "deceased" [19, 20]. Patients who deceased within 30 days of their FSA were described as having "rapid decline".

The data was recorded anonymously in excel. Ethics approval was given by the internal Oncology Service ethics review committee in the Canterbury Regional Cancer and Haematology Service. Maori consultation was undertaken with the University of Otago Christchurch advisor, Karen Keelan. Patient characteristics were described as simple tables, with Chi square statistics used to determine influence of factors on outcome at 3 and 6 months. A two tailed p-value was used to indicate statistical significance with no adjustment for multiple comparisons.

Results

A total of 305 patients aged 75 years and older attended a FSA in the Medical Oncology Service, Christchurch Hospital, between 1 June 2016 and 1 June 2017. A further 45 were referred, but did not attend,

accounted for by 23 who declined the appointment or had opted for symptomatic care, 15 deceased before the appointment date, and seven unknown or other reasons. Failure to attend was not related to age group, but 88.9% had locally advanced (17.8%) or metastatic (71.1%) disease.

The number attending according to age group, gender, disease stage and ethnicity is shown in (Table 2), with cancer diagnosis, together with that of non-attendees, shown in (Table 3).

Table 2: Characteristics of all referrals, and of those who attended an FSA.

		Total number referred (%)	Attended FSA (%)
Total		345	305
Gender	Male	182 (52)	156 (51.1)
	Female	168 (48)	149 (48.9)
Age, years	75-79	176 (50.3)	149 (48.9)
	80-84	113 (34.9)	103 (33.8)
	85+	61 (14.8)	53 (17.3)
Stage	Local (adjuvant)	39 (11.2)	38 (12.5)
	Locally advanced	119 (34)	111 (36.4)
	Metastases	188 (53.7)	156 (51.1)
	Not known	4 (1.1)	0 (0)
BMI, kg/m^2	<18.5		5 (1.6)
	18.5-24.9		107 (35.1)
	25-29.9		103 (33.8)
	>29.9		64 (21)
	Unknown		26 (8.5)
Ethnicity	NZ European	335 (95.7)	292 (95.7)
	Māori	8 (2.3)	7 (2.3)
	Asian	4 (1.1)	4 (1.3)
	Other	3 (0.9)	2 (0.7)
Prescribed drugs	>3/day		176 (57.7)
	<4/day		110 (38.5)
	Unknown		19 (6.2)
Domicile	Own home		158 (51.8)
	Hospital		16 (5.2)
	Retirement home		7 (2.3)
	Unknown		124 (40.7)
Frailty, G6	Frail, 10 or less		169 (55.4)
	Not frail >10		108 (35.4)
	Unknown		28 (9.2)

Table 3: Cancer diagnoses of referred patients.

		Referred (%)	Attended FSA (%)	Non-attenders (% of referred)
Diagnosis	Colorectal	99 (28.3)	90 (29.5)	9 (10.0)
	Lung	35 (10.0)	30 (9.8)	5 (14.3)
	Melanoma	35 (10.0)	28 (9.2)	7 (20.0)
	Breast	34 (9.7)	31 (10.2)	3 (8.8)
	Prostate	31 (8.5)	28 (9.2)	3 (9.7)
	Lymphoma	26 (7.4)	21 (6.9)	5 (19.2)
	Gastro-oesophageal	22 (6.3)	19 (6.2)	3 (13.6)
	Gynaecologic	20 (5.7)	19 (6.2)	1 (5.0)
	Pancreas	10 (2.8)	7 (2.3)	3 (30.0)
	Brain	8 (2.3)	7 (2.3)	1 (12.5)
	Other	28 (8.0)	25 (8.2)	3 (10.7)
Total		350	305	45

Considering those 305 people who attended an FSA, the mean age was 80.5 years, with 11.2% referred for adjuvant therapy, 34% for treatment of locally advanced disease, and 53.7% for distant metastases. Colorectal cancer made up 28.3% of referrals seen, with lung (10.0%), melanoma (10.0%) and breast (9.7%) next most common. Pancreas cancer diagnosis had the greatest proportion not attending, 30% of referrals,

followed by melanoma (19.2%) and lymphoma (20%). One third of those seen at FSA were of normal weight, and half were overweight (33.8%) or obese (21.0%), fewer than 2% underweight, while BMI was not available for 8.5%. Just over half were taking four or more prescription drugs daily. At least half were still living in their own home, but the living situation was not recorded for 40%. Treatment received by the 305 who attended their FSA was surgery in 46.9%, chemotherapy in 37.7%, radiation in 31.5%, endocrine therapy in 11.1%, targeted therapy in 8.8%, and other therapy in 1.0%. Some patients received more than one modality.

The mean peripheral blood neutrophil count at diagnosis was 5.85 x 10^9/L (range 1.4 to 27.6), and lymphocyte count 1.99 x 10^9/L (range 0.4 to 70.4), with mean N/L ratio 4.42 (range 0.10 to 28.67). Data was not available for 44 patients, however. Information was not available for nutritional intake in 186 patients, and neuropsychiatric assessment in 254 patients. Using the G8 criteria excluding nutritional and neuropsychiatric status, as the G6 score, with a score cut-off of 10, 55.4% were deemed frail, 35.4% not frail, with missing data for 9.2%. The missing data in 28 patients included no height in 24, meaning also no BMI, no weight in 15, no mobility data in 9, no weight loss information in 4. Figure 1 shows disease status for all those who attended their FSA, after 3 months and 6 months, according to frailty using G6 score. Thirteen patients were deceased within 30 days of their attendance at their FSA, showing a rapid decline. Nearly half had died or were less well by 6 months (46.2%). A small proportion 11.8% had improved by 6 months. There were 61 unevaluable at 3 months and 93 at 6 months.

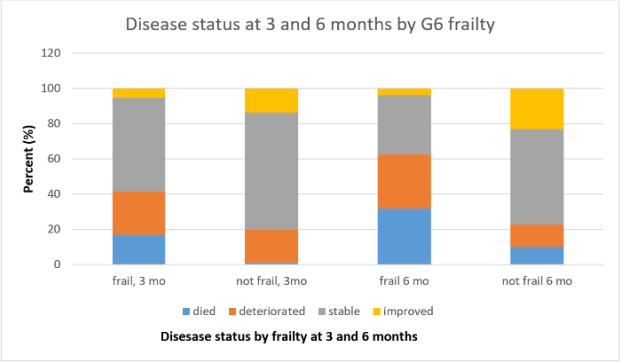

Figure 1: Disease status at 3 and 6 months according to frailty by G6 score.

Table 4: Demographic factors and treatment, associations with outcome at 3- and 6-months follow-up, Pearson Chi-Square test.

	3 months		**6 months**	
	Number	Chi^2 p-value	Number	Chi^2 p-value
Age	244	0.207	212	**0.038***
Ethnicity	244	0.352	212	0.579
Gender	244	0.782	212	0.672
BMI#	228	0.659	198	0.599
G8 BMI	228	0.375	198	0.641
>3 medications	232	**0.041***	202	0.583
Frail, G7(12)	235	**0.010***	204	**<0.001*****
Frail, G6(10)	227	**<0.001*****	197	**<0.001*****
Coded living	243	0.722	211	0.332
Diagnosis	244	0.087	212	**0.011***
Stage	244	**0.001****	212	**<0.001*****
N/L quartiles	230	0.395	198	**0.003****
N/L<4	230	0.064	198	**0.001*****
Treatment				
Chemotherapy	244 (112)	**<0.001*****	212 (95)	**<0.001*****
Radiation	244 (88)	0.146	212 (70)	**0.005****
Endocrine	244 (26)	**0.018***	212 (26)	**0.004****
Targeted	244 (25)	0.385	212 (25)	0.595
Surgery	244 (98)	0.051	212 (98)	**0.001*****
Other	244 (3)	0.550	212 (3)	0.621

WHO BMI categories

Frail by G7 score is 12 and below, and G6 score 10 and below

*p<0.05

**p<0.01

***p<0.001

Outcome at 6 months was significantly (p<0.05) associated with age, frail G6 score (10 or lower), type of cancer, tumour stage, use of chemotherapy, endocrine therapy, radiation, and surgery, as well as N/L ratio less than 4 (Table 3). Of those frail by G6 score, 62.7% had died or deteriorated by 6 months, compared with 22.9% of those not frail (Figure 1), with stable disease for 33.6% frail and 54.0% not frail. At 6 months, 23.0% of those not frail had improved, compared with 3.6% of those who were frail. To further explore reducing score items criteria from 8

(G8 score), the 7-item G7 score was determined, defined as G8 without a neuropsychiatric score (scored 0, 1 or 2), with frailty score cut off of 12 or less (Table 3). This was significantly associated with outcome at both 3 and 6 months. However, G6 score of frailty was associated with a higher proportion less well or deceased at 3 and 6 months, suggesting it may be more useful.

The greatest proportion of patients were deceased at 6 months for cancers of pancreas (83.3%), melanoma (41.7%), lung (35.0%), followed by grouped uncommon types (29.4%), colon (25.0%) and brain (25.0%), then the remaining types 14% or less. At 6 months, 34.4% with metastatic disease had died, with 25.0% deteriorated, a total of 59.4%. Importantly, 26.1% of those referred for adjuvant therapy for early, localised disease had died by 6 months. Use of chemotherapy, radiation therapy or endocrine therapy was associated with better outcome at 6 months, though this may reflect fitness to receive these treatments and cancer type and stage. Considering those who received chemotherapy, 9.5% had died within 6 months, 24.2% deteriorated, 51.6% stable and 14.7% improved, while 37.6% of those not receiving chemotherapy had died. Of the 26 patients who received endocrine therapy, none had died within 6 months. There was no significant difference at 6 months for the 25 receiving targeted therapies, compared with not. Surgery was associated with a better 6-month outcome than no surgery, 14.3% deceased compared with 34.2%, and 67.3% improved or stable compared with 42.1%. Neutrophil/lymphocyte (N/L) ratio by quartiles was significantly associated with outcome (Chi-Square test) (Table 3), with deaths by 6 months 39.1% for N/L greater than 5.3, compared with 14.9% for <2.13. Non-parametric analysis of variance confirmed that the G6 score and N/L at referral were each strongly associated with outcome at 6 months, $p<0.001$ and $p<0.003$ respectively.

Table 5: Referrals and treatment used according to age group, and disease status at 3 and 6 months, as percent within age group, Pearson Chi-Square test.

	Number	% of 75-79 years	% of 80-84 years	% of >84 years
Attend FSA	305	84.7	90.2	88.5
Females	168	52.3	43.4	44.2
4+ drugs/day	305	35.6	38.2	32.6
Surgery	305	49.7	50.0	30.4*
Chemotherapy	305	49.7	30.0	17.4**
Endocrine Rx	305	12.1	10.9	8.7
Targeted Rx	305	8.1	9.1	10.9
Radiation	305	35.6	27.3	28.3
3 months died	244	10.2	10.7	25.0
3 months deteriorated	244	18.8	22.6	21.9
6 months died	212	20.0	27.1	40.7
6 months deteriorated	212	20.0	27.1	11.1***

*p<0.05
**p<0.01
***p=0.03

Age did not influence attendance versus not at FSA (Table 5). Gender and use of four or more prescription drugs did not vary by age group (Table 5). Chemotherapy and surgery were used more often in younger age groups, but there was no difference by age group for use of endocrine therapy, targeted therapy or radiation. For age group, 40.7% older than 84 years had died by 6 months, compared with 20.0% aged 75-80 years (Table 5). More than half (51.8%) were either deceased or deteriorated by 6 months if older than 84 years.

Discussion

This audit showed that in our population of patients newly referred to the medical oncology service with a new cancer diagnosis who were aged 75 years and older, half were in the 75-79 age group, and the remainder 80 years and older. Half of those aged over 84 years had deteriorated or died (40%) within 6 months, compared with 40% (includes 20% died) aged 75-79 years. Pancreas cancer had the highest mortality at 6 months, 83%, with melanoma 42% and lung cancer 32%, demonstrating the importance of cancer type. There was less use of surgery over 84 years and less chemotherapy over 80 years, but use of targeted therapies, radiation and endocrine therapies did not change with advanced age.

Most items in the G8 score were well recorded, but two items were not recorded routinely, with nutritional status recorded in 39% and neuropsychiatric assessment in 17%, limiting use of the G8 score retrospectively. However, a simple G6 frailty score, adapted from the well validated G8 score was associated with outcome at 3 and 6 months [8,9]. The G8 score separates non-frail patients from frail patients who need additional assessment for reversible factors and who are less likely to perform well on intensive therapies. This information could assist patients, their families and clinical team reach the best decision for them around their management and treatment options. The G8 should be prospectively applied, including the additional items which were not uniformly available in this retrospective audit, to confirm validity in our population, and test the shorter G6 score.

Assessing patients at presentation, the G6 score and tumour stage were both associated with outcome at 3 and 6 months, and cancer diagnosis, age and N/L ratio associated with outcome at 6 months. Neutrophil/lymphocyte (N/L) ratio in peripheral blood will need more study to explore its contribution over other prognostic factors. Treatment was decided after clinical assessment, so reflects also the impact of clinical decision-making. Surgery and the oncology treatments used

were associated with outcome at 6 months, but inevitably this is confounded by diagnosis and stage. Immunotherapy was used in only a few patients due to funded indications in New Zealand. Endocrine therapy in breast and prostate cancer as expected was associated with good outcomes at 3 and 6 months.

A simple performance status and response characterisation was used to assess patients at 3 and 6 months. The categories closely matched those used frequently in palliative care to assess phase of illness [19]. Our categories retained "stable", combined unstable and deteriorating into a single one of "deteriorated", used "deceased" instead of "dying", and added "improved" for those with better status at follow-up. While not validated in this population, it was simple to apply on review of medical records in a real-world population where formal response criteria were not available for many patients, especially when managed palliatively. As expected in this elderly population rapid decline between referral and planned first assessment, was prognostic of poor outcome, since performance status, cancer stage or biology usually precluded intensive therapy. Most had been discussed with their referring clinicians, but this audit highlights the potential to enhance this interaction to avert futile FSAs.

The contribution of factors of the G6 score over and above age were considered, referring to the G8 score [8]. Patients who were over 85 years scored 0, and if they fell short on any two (or severely on just one) of food intake (decreased or severely decreased), mobility (chair/bed bound, mobile but don't go out, or go out), health compared to peers, BMI (best if >23 Kg/m^2), or needed more than three medications per day, would reach a frail score of 10 or lower. If aged between 80 and 85 years, they could fall short on one more item or severity grade, and if below 80 years, had one more score point they could fail. Thus, the modified G6 offered additional information over age alone, which was easy to obtain on taking a history, height and weight from the patient.

In this New Zealand population, there were very few Māori, but this may be because the proportion of Māori is less at older ages due to their poorer health status, and as discussed in our pre-audit Māori research consultation, we would need to audit a younger cohort of newly diagnosed Māori. Strengths of this study are its "real world" patient population, with all referrals accounted for. The population were the most senior aged 75 years and over, who are often the most challenging group for whom to reach therapy decisions. The G6 score was simple to apply, based on usually collected clinical information, but would need more intensive application to obtain a G8 score. Weaknesses are the inclusion of all cancer types and stages, with inherently different prognoses, and different possible therapies, with some more tolerable for a senior population, e.g. endocrine therapies. The omission of the two items from the G8 score may be less important if the clinicians are taking into account history they obtain of recent reduction of nutritional status and neuropsychiatric problems when they advise the patient.

We propose that using a modified G6 score may be useful, and should be prospectively explored, and helped identify senior patients presenting with a new cancer diagnosis who would have a poorer outcome with intensive therapy. The components of the score extend the use of age alone, to include weight and height (BMI), loss of appetite, decreased mobility, self-declared health status relative to peers, and more than three regular prescribed medications. The cancer diagnosis and stage, and benefit from medical oncology therapies should also be considered in reaching a shared decision about the treatment plan.

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Conflicts of interest

None.

REFERENCES

1. Stats NZ (2019) Wellington: New Zealand Government.
2. Ministry of Health (2019) Wellington: New Zealand Government.
3. Sternberg SA, Wershof Schwartz A, Karunananthan S, Bergman H, Mark Clarfield A (2011) The identification of frailty: a systematic literature review. *J Am Geriatr Soc* 59: 2129-2138. [Crossref]
4. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C et al. (2001) Frailty in older a dults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 56: M146-M56. [Crossref]
5. Extermann M, Boler I, Reich RR, Lyman GH, Brown RH et al. (2012) Predicting the risk of chemotherapy toxicity in older patients: The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. *Cancer* 118: 3377-3386. [Crossref]
6. Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD et al. (2011) Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. *J Clin Oncol* 29: 3457-3465. [Crossref]
7. Droz JP, Balducci L, Bolla M, Emberton M, Fitzpatrick JM et al. (2010) Management of prostate cancer in older men: recommendations of a working group of the International Society of Geriatric Oncology. *BJU Int* 106: 462-469. [Crossref]
8. Droz JP, Aapro M, Balducci L, Boyle H, Van den Broeck T et al. (2014) Management of prostate cancer in older patients: updated recommendations of a working group of the International Society of Geriatric Oncology. *Lancet Oncol* 15: e404-e414. [Crossref]
9. Bellera CA, Rainfray M, Mathoulin-Pelissier S, Mertens C, Delva C et al. (2012) Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. *Ann Oncol* 23: 2166-2172. [Crossref]
10. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 40: 373-383. [Crossref]
11. Ferrat E, Paillaud E, Caillet P, Laurent M, Tournigand C et al. (2017) Performance of four frailty classifications in older patients with cancer: prospective elderly cancer patients cohort study. *J Clin Oncol* 35: 766-777. [Crossref]
12. Walsh SR, Cook EJ, Goulder F, Justin TA, Keeling NJ et al. (2005) Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. *J Surg Oncol* 91: 181-184. [Crossref]
13. Li M, Liu X, Zhang X, Zhang JF, Wang WL et al. (2014) Prognostic role of neutrophil-to-lymphocyte ratio in colorectal cancer: a systematic review and meta-analysis. *Int J Cancer* 134: 2403-2413. [Crossref]

14. Ozyurek BA, Ozdemirel TS, Ozden SB, Erdogan Y, Kaplan B et al. (2017) Prognostic value of the neutrophil to lymphocyte ratio (NLR) in lung cancer cases. *Asian Pac J Cancer Prev* 18: 1417-1421. [Crossref]
15. Guthrie GJ, Charles KA, Roxburgh CS, Horgan PG, McMillan DC et al. (2013) The systemic inflammation-based neutrophil–lymphocyte ratio: experience in patients with cancer. *Crit Rev Oncol Hematol* 88: 218-230. [Crossref]
16. Yu Y, Qian L, Cui J (2017) Value of neutrophil-to-lymphocyte ratio for predicting lung cancer prognosis: A meta-analysis of 7,219 patients. *Mol Clin Oncol* 7: 498-506. [Crossref]
17. Li J, Chen Q, Luo X, Hong J, Pan K et al. (2015) Neutrophil-to-lymphocyte ratio positively correlates to age in healthy population. *J Clin Lab Anal* 29: 437-443. [Crossref]
18. WHO Consultation on Obesity: preventing and managing the global epidemic: report of a WHO consultation. WHO Technical Report series, 894. ISBN 92 4 120894 5, ISSN 0512-3054.
19. Masso M, Allingham SF, Banfield M, Johnson CE, Pidgeon T et al. (2015) Palliative Care Phase: inter-rater reliability and acceptability in a national study. *Palliat Med* 29: 22-30. [Crossref]
20. Mather H, Guo P, Firth A, Davies JM, Sykes N et al. (2018) Phase of illness in palliative care: cross-sectional analysis of clinical data from community, hospital and hospice patients. *Palliat Med* 32: 404-412. [Crossref]