Published in final edited form as:

J Geriatr Oncol. 2013 July ; 4(3): 227–234. doi:10.1016/j.jgo.2013.02.002.

Geriatric assessment is associated with completion of chemotherapy, toxicity and survival in older adults with cancer

Tanya M. Wildes, MD¹, Alexander P. Ruwe¹, Chloe Fournier¹, Feng Gao, PhD², Kenneth R. Carson, MD¹, Jay F. Piccirillo, MD³, Benjamin Tan, MD¹, and Graham A. Colditz, MD, DrPH⁴

¹Division of Medical Oncology, Washington University School of Medicine

²Division of Biostatistics, Washington University School of Medicine

³Department of Otolaryngology and Outcomes Research, Washington University School of Medicine

⁴Department of Surgery, Washington University School of Medicine

Abstract

Objectives—Our purpose was to determine whether geriatric assessments are associated with completion of a chemotherapy course, grade III/IV toxicity or survival in older adults with cancer.

Materials and Methods—In this prospective cohort study, patients aged 65 years and older with colorectal, lung, or breast cancer or lymphoma completed a brief geriatric assessment prior to chemotherapy. Endpoints included completion of the planned number of chemotherapy cycles, grade III/IV toxicity and survival. Multivariate logistic regression determined which factors were independently associated with completion of therapy, grade III/IV toxicity or death.

Results—Sixty-five patients were enrolled in the study. The median age was 73 years (range 65–89). Geriatric syndromes were common, including depression (21.5%), dependence on others to carry out instrumental activities of daily living (38.5%) and activities of daily living (10.8%), and comorbidities (mild 47.7%, moderate 20%, severe 15.4%). Of the 65 participants, 67.6% completed the planned number of chemotherapy cycles. Curative intent therapy [OR 4.97 (95% CI 1.21–18.81)], Eastern Cooperative Oncology Group (ECOG) performance status 2–3 [OR 0.089 (0.015–0.53)] and renal function [OR 1.03 (1.00–1.06) per ml/min] were significantly associated with therapy completion. Furthermore, 31.1% experienced grade III/IV non-hematologic toxicity. Moderate to severe comorbidities significantly increased the risk of grade III/IV non-hematologic toxicity [OR 6.13 (1.65–22.74)]. Patients who received chemotherapy with curative intent had lower mortality [HR 0.15 (0.06–0.42)], while patients who reported a fall in the month prior to chemotherapy had an increased risk of death [HR 3.20 (1.13–9.11)].

Conclusions—Geriatric assessment is associated with completion of a planned number of cycles of chemotherapy, grade III/IV non-hematologic toxicity and mortality.

Keywords

Aging; geriatrics; geriatric assessment; chemotherapy; cancer; toxicity; survival

Corresponding author: Tanya Wildes, Washington University School of Medicine, 660 South Euclid Ave, Campus Box 8056, St Louis MO 63110 USA, Phone (314) 362-5654, Fax (314) 362-5123, twildes@dom.wustl.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

The incidence of most cancers increases with age. With the aging of the population, a 67% increase in cancer incidence in older adults in the United States is expected by the year 2030.(1) Numerous studies have shown that older adults are undertreated.(2–4) This may be, in part, due to concerns about a greater risk of treatment toxicity in older adults. Decision-making regarding older adults is also challenging due to the underrepresentation of older adults in clinical trials, and the frequent occurrence of comorbidities, functional limitations or other geriatric syndromes, which may influence a clinician's estimate of the risk of therapy and their decision to recommend chemotherapy.(5) Unfortunately, standard oncology assessments do not routinely assess certain geriatric parameters, including depression, cognition, functional decline, falls, and polypharmacy.

Two recent prospective cohort studies have demonstrated the utility of a geriatric assessment in older adults with cancer in predicting tolerance of chemotherapy.(6,7) In the Cancer and Aging Research Group (CARG) study, geriatric assessment parameters including hearing impairment, falls, requiring assistance with medications, decreased ability to walk one block and decreased social activity were associated with an increased risk of grade III or greater toxicity with chemotherapy.(8) In the study by Extermann *et al.*, geriatric parameters were also predictive of chemotherapy toxicity. Instrumental activities of daily living predicted grade III or greater hematologic toxicity, while poor performance status, impaired cognition and nutritional impairment predicted grade III or greater non-hematologic toxicity.(7)

Completion of chemotherapy is also an important consideration in counseling older adults regarding the use of chemotherapy. In both the curative-and palliative-intent settings, estimating the benefit of chemotherapy is predicated on the patient completing the planned course of chemotherapy. Failure to complete a course of chemotherapy may be associated with poorer outcomes. Regarding patients with colorectal cancer, completion of adjuvant chemotherapy is associated with lower cancer-related mortality.(9) Given that some patients will discontinue therapy, even in the absence of grade III/IV toxicity, determining which patients are less likely to complete a planned course of therapy will assist patients and clinicians in making decisions regarding chemotherapy and allow subsequent intervention to improve rates of completion of therapy among older adults with cancer. Finally, geriatric assessment is predictive of early mortality in older patients with cancer (10); thus, ascertaining which older adults are at increased risk for mortality will further aid the decision-making process.

In this study, we sought to examine which geriatric assessment parameters were associated with completion of a planned course of chemotherapy, grade III/IV hematologic and non-hematologic toxicity of chemotherapy, and survival.

METHODS

The Washington University School of Medicine Human Studies Committee approved this prospective study. Informed consent was obtained from patients age 65 or older with a biopsy-proven malignancy of the lung, breast, colon/rectum or lymphoma, who were likely to begin a course of chemotherapy. Patients receiving concurrent radiation therapy were excluded. Potential study candidates were identified from the patients who were seeking initial consultation or continued treatment with a medical oncologist at the Siteman Cancer Center. Convenience sampling was used for this study as the subjects were not consecutive.

Prior to initiation of a course of chemotherapy, subjects completed a brief geriatric assessment. The assessment included items on basic demographics, falls within the past month, the presence of a caregiver, living conditions, medications and several geriatric

assessment measures, including a validated measure of depression (Center for Epidemiologic Studies – Depression).(11) Medications considered inappropriate in the elderly were noted using Beers Criteria.(12) The Short Blessed Test(13) was administered by the research team to assess cognition. On this test, scores >9 are indicative of the need for further evaluation of cognition. Members of the healthcare team also assessed the Eastern Cooperative Oncology Group (ECOG) performance status.(14) Functional status was assessed using the Katz Index of Daily Living(15) and the Lawton Index of Instrumental Activities of Daily Living (IADL) (16). Nutritional risk was assessed using the Mini Nutritional Assessment-short form.(17) Comorbidities were ascertained through medical record review and captured using the Adult Comorbidity Evaluation, ACE-27, comorbidity index.(18) Baseline laboratory parameters, including the glomerular filtration rate as estimated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation(19), were obtained. The planned chemotherapeutic regimen, including chemotherapeutic agents and the number of cycles, was specified at the time of the initial geriatric assessment.

The primary outcome examined in this study was completion of the planned number of cycles of chemotherapy. Secondary outcomes included the occurrence of National Cancer Institute Common Toxicity Criteria Grade III/IV toxicity (hematologic and non-hematologic), and overall survival. Toxicities were ascertained via medical record review at the completion of the study and graded by one individual. If treatment was terminated prior to completion of the planned number of cycles of therapy, the reason for cessation was noted.

STATISTICAL ANALYSIS

Baseline demographics and geriatric assessments were summarized using descriptive statistics. Those who completed chemotherapy were compared with those who did not using either a Student t-test, Mann-Whitney non-parametric rank-sum test, Fisher's exact or Chi-square test as appropriate. Multivariate logistic regression was performed to identify potential independent risk factors for the inability to complete the planned course of chemotherapy, and grade III/IV toxicity; stepwise forward selection was used considering variables with a $p < 0.10$ on univariate analysis. Taking a similar strategy, univariate and multivariate Cox proportional hazards models were fitted to assess the independent effects of patient, disease, and geriatric assessment parameters on overall survival. Overall survival was defined as the time from the date of the initial geriatric assessment until death, censored at the last clinical contact. All analyses were two-sided and significance was set at a p -value of 0.05. Statistical analyses were performed using SAS (SAS Institutes, Cary NC).

RESULTS

From July 2008 to February 2012, 65 patients were enrolled. Baseline demographic and laboratory values are presented in Table 1. Geriatric syndromes were common, as shown in Table 2. Several chemotherapeutic and immunochemotherapeutic regimens were represented for each disease site. Regimens included FOLFOX with or without cetuximab (N=18), capecitabine and oxaliplatin (N=3), capecitabine alone (N=3), docetaxel and cyclophosphamide with or without trastuzumab (N=5), doxorubicin and cyclophosphamide followed by docetaxel (N=2), epirubicin and cyclophosphamide (N=2), rituximab-cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP, N=7), rituximab-cyclophosphamide, vincristine and prednisone (R-CVP, N=2), doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD, N=1), dose-adjusted rituximab, etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin (DA-R-EPOCH, N=1), rituximab-methotrexate (N=1), rituximab, cyclophosphamide and fludarabine (N=1), rituximab bendamustine (N=1), cisplatin-vinorelbine (N=1), carboplatin-pemetrexed (N=3),

pemetrexed alone, (N=1), carboplatin-etoposide (N=1), etoposide (N=1), and a clinical trial therapy (N=7). One patient received an initial dose-reduction for renal impairment.

Two-thirds (44/65) of patients completed the planned number of cycles of chemotherapy; 26.2% (17/65) did not complete the course of chemotherapy, while 6.2% (4/65) never started due to patient preference. Of the seventeen who did not complete therapy, 64.7% (11/17) of cessations were due to toxicity from chemotherapy, 17.6% (3/17) were due to patient preference, and 17.6% (3/17) were due to cancer progression. Of the 61 patients who started therapy, 31.1% (19/61) experienced grade III/IV non-hematologic toxicity, 26.2% (16/61) experienced grade III/IV hematologic toxicity, and 41% (25/61) experienced either grade III/IV non-hematologic or hematologic toxicity.

On univariate analysis, factors associated with completion of the planned course of chemotherapy included falls, intent of therapy, ECOG performance status 2–3, age, and creatinine clearance (Table 3). On multivariate analysis, variables with $p > 0.1$ were considered in stepwise forward selection. In the multivariate model, intent of therapy, performance status, and renal function were associated with completion of chemotherapy. For patients undergoing chemotherapy with curative intent, their odds of completing chemotherapy were higher by nearly five. The odds of completing chemotherapy were lower for patients with an ECOG performance status of 2–3 [Odd Ratio (OR) 0.089, 95% Confidence Intervals (CI) 0.015–0.530], while creatinine clearance was associated with a 3% increase in odds of completing chemotherapy per milliliter per minute.

Factors associated with grade III/IV non-hematologic toxicity on univariate analysis included female gender, depression, comorbidities, and body mass index (Table 4). On multivariate analysis, the presence of moderate to severe comorbidities was associated with higher odds (6.13 to 1) of experiencing grade III/IV non-hematologic toxicity [OR 6.13 (95% CI 1.65–22.74), $p = 0.007$]. The odds for experiencing grade III/IV non-hematologic toxicity was lower for females compared to males [OR 0.20 (95% CI 0.01–0.75), $p = 0.017$]. However, when analyses excluded patients with breast cancer, gender no longer predicted non-hematologic toxicity ($p = 0.14$).

None of the variables studied predicted grade III/IV hematologic toxicity. Comorbidities were the only variable associated with any (either hematologic or non-hematologic) grade III/IV toxicity [OR 3.79 (1.25–11.51), $p = 0.019$].

At a median follow-up of 20 months (range 0.01–47 months), 22 patients (34%) in the whole cohort had died. There were no deaths attributed to chemotherapy toxicity. On univariate analysis, factors associated with mortality included a diagnosis of lung cancer, falls, intent of therapy (curative versus palliative), and age (Table 5). On multivariate analysis, curative intent of chemotherapy was associated with an 85% lower risk of death [HR 0.15 (95% CI 0.06–0.42), $p < 0.001$]. Falls were associated with a three-fold greater risk of mortality [HR 3.2 (95% CI 1.13–9.11), $p = 0.029$].

DISCUSSION

Our study adds to the growing body of literature supporting the importance of geriatric assessment in older adults with cancer. In this small prospective cohort study, geriatric assessment parameters were associated with completion of a planned course of chemotherapy, grade III/IV non-hematologic toxicity, and mortality.

The primary outcome in our study was completion of a planned course of chemotherapy. This outcome differs subtly from studies assessing grade III/IV toxicity of chemotherapy. In our study, nearly 20% of discontinued chemotherapy was due to patient preference, in the

absence of grade III/IV toxicity. What is more, others who experienced grade III/IV toxicity completed the planned course of chemotherapy. Completion of chemotherapy as an endpoint allows the clinician to estimate the magnitude of benefit of chemotherapy. In a randomized trial of vinorelbine with or without gemcitabine in older adults with non-small cell lung cancer, comorbidities were more predictive of early termination of chemotherapy than performance status.(20) In a Surveillance, Epidemiology and End Results (SEER) Program - Medicare analysis of older women with ovarian cancer, aged 75 and up, comorbidities and single marital status were associated with incomplete courses of chemotherapy.(21) In our study, patients who had either palliative chemotherapy, an ECOG performance status of 2 or greater, or lower renal function were less likely to complete a planned course of chemotherapy.

Other studies have demonstrated the utility of geriatric assessment in predicting grade III/IV toxicity of chemotherapy in older adults with cancer. In a prospective cohort study of older women with advanced ovarian cancer, the results showed that depression, poor performance status, and dependence independently predicted severe toxicity of chemotherapy.(22) CARG developed a largely self-administered geriatric assessment to predict toxicity of chemotherapy.(6) In their 500 patient cohort of adults age 65 and older, predictors of grade III/IV toxicity, including patient age, tumor/treatment variables, laboratory values and geriatric assessment parameters, were combined to create a model. In their model, the geriatric assessment parameters that were predictive of chemotherapy toxicity included hearing impairment, falls within the past six months, requiring assistance with medications, decreased ability to walk one block, and decreased social activities. Other variables included patients aged 72 and older with the presence of genitourinary or gastrointestinal cancer, who had standard chemotherapy doses, combination chemotherapy, anemia or low creatinine clearance.

In the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) trial, over 500 patients with various malignancies receiving chemotherapy underwent a baseline geriatric assessment prior to chemotherapy.(7) Two different models were created: one for hematologic and one for non-hematologic toxicity. Hematologic toxicity was independently predicted by diastolic blood pressure over 72 mmHg, dependence in IADLs, elevated serum lactate dehydrogenase and chemotoxicity (a measure of the frequency of grade III/IV toxicity for the specific regimen in published clinical trials). In our study, none of our variables were significantly associated with hematologic toxicity. Of note, we did not evaluate prophylactic colony-stimulating factor use, which may have influenced the rate of hematologic toxicity in our cohort. In the CRASH study, predictors of non-hematologic toxicities were ECOG performance status, cognitive impairment, nutritional risk, and chemotoxicity. Grade III/IV non-hematologic toxicity in the present study was associated with male gender and moderate to severe comorbidities. This gender difference was likely driven by the large proportion of women receiving well-tolerated adjuvant chemotherapy for breast cancer, as it was not seen when analyses excluded patients with breast cancer.

The rate of toxicities in our study was lower than that noted in the CARG(6) and CRASH(7) studies. While the rate of grade III/IV hematologic toxicities in our study was similar to the former studies (26% in our study versus 26% and 32%, respectively), our rate of non-hematologic toxicity was lower (31% versus 43% and 56%, respectively). This may reflect differences in the study cohorts; for example, in the CRASH study, all enrolled patients were age 70 or older, whereas our cohort was slightly younger, with enrollment beginning at age 65. Indeed, in the CRASH study, only 49% of patients completed therapy, compared with 67% in our cohort. Alternatively, our ascertainment of toxicity through medical record review may have underestimated the incidence or severity of toxicities.

Geriatric assessment can also predict survival in older patients with cancer. In a prospective cohort study of adults over age 70, who were to begin a course of chemotherapy, factors independently associated with early death included male gender, advanced tumors, nutritional compromise, and impaired physical function on the Timed Up and Go test, which is a performance-based test that assesses proximal muscle strength, gait and balance.(10) In our study, palliative intent of chemotherapy and falls in the past month were associated with mortality. The utility of falls as a predictor of mortality has merit, as falls are associated with sarcopenia,(23) which is associated with inflammatory markers, frailty and mortality.(24,25)

Strengths of this study include the fact that geriatric assessment parameters were prospectively obtained prior to initiation of chemotherapy. This allowed for the evaluation of geriatric domains that are not routinely assessed in oncology practice. Because assessments were completed prior to initiation of chemotherapy, they reflected the patient's baseline health rather than toxicities of therapy.

There are a number of limitations in this small cohort study. First, the sample size limits the power of the multivariate analysis. For example, there were significant associations between three of the variables and the completion of therapy on the multivariate analysis. As there were only 17 patients who did not complete chemotherapy, statistical simulation studies suggest that no more than two predictors (one for every ten events) be included in the model.(26) However, recent simulation studies suggest that the dogmatic "rule of 10s", that is, that there must be 10 events per predictor variable in multivariate analysis, may be relaxed, with 5–9 events per predictor variable performing similar to 10 or more events per predictor variable in the model.(27)

The inclusion of several types of cancer and different chemotherapeutic regimens is also a limitation; geriatric factors may have differential prognostic impact in different malignancies. Kallogjeri *et al.* showed that individual comorbid conditions have different prognostic impacts in various malignancies.(28) Models of chemotherapy completion and toxicity may differ from ours if studied in an individual malignancy. Another limitation is lack of data on dose reductions and delays. We did not collect data on dose reductions or dose delays, and thus, are unable to comment on reduced dose intensity, which may impact effectiveness of therapy, even if the planned number of cycles is completed.

One final limitation is insensitivity of the geriatric assessment measures selected in this study. Some likely had ceiling effects in the population studied. For example, only 5% of patients in our cohort screened positive for cognitive impairment with the Short Blessed Test, while other studies have found almost 30% of older adults with cancer had an abnormal Mini Mental Status Exam.(29) In addition, the Mini-Nutritional Assessment was less informative in our population given the high prevalence of overweight/obesity.

In conclusion, our study adds to the evidence that geriatric assessment has utility regarding older adults with cancer. We demonstrated that geriatric assessment parameters were associated with completion of a planned course of chemotherapy, grade III/IV non-hematologic toxicity, and mortality. Future studies are needed to evaluate the nuances of utility for geriatric assessment in helping patients and providers predict chemotherapy treatment completion, tolerance of therapy and mortality in older adults for a more informed decision-making process.

Acknowledgments

This publication was made possible by Grant Number KM1CA156708-01 through the National Cancer Institute (NCI) at the National Institutes of Health (NIH) and Grant Numbers UL1 TR000448, KL2 TR000450, TL1 TR000449 through The Clinical and Translational Science Award (CTSA) program of the National Center for

Advancing Translational Sciences at the National Institutes of Health. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCATS or NIH. The authors wish to acknowledge the support of the Biostatistics Core, Siteman Comprehensive Cancer Center and NCI Cancer Center Support Grant P30 CA091842.

REFERENCES

1. Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of Cancer Incidence in the United States: Burdens Upon an Aging, Changing Nation. *Journal of Clinical Oncology*. 2009 Jun 8; 27(17):2758–2765. [PubMed: 19403886]
2. Bouchardy C, Rapiti E, Fioretta G, Laissue P, Neyroud-Caspar I, Schäfer P, et al. Undertreatment strongly decreases prognosis of breast cancer in elderly women. *J. Clin. Oncol*. 2003 Oct 1; 21(19): 3580–3587. [PubMed: 12913099]
3. Sundararajan V, Hershman D, Grann VR, Jacobson JS, Neugut AI. Variations in the use of chemotherapy for elderly patients with advanced ovarian cancer: a population-based study. *J. Clin. Oncol*. 2002 Jan 1; 20(1):173–178. [PubMed: 11773167]
4. Mahoney T, Kuo YH, Topilow A, Davis JM. Stage III colon cancers: why adjuvant chemotherapy is not offered to elderly patients. *Arch Surg*. 2000 Feb; 135(2):182–185. [PubMed: 10668878]
5. Extermann M, Chen H, Cantor AB, Corcoran MB, Meyer J, Grendys E, et al. Predictors of tolerance to chemotherapy in older cancer patients: a prospective pilot study. *Eur. J. Cancer*. 2002 Jul; 38(11): 1466–1473. [PubMed: 12110492]
6. Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD, Gross CP, et al. Predicting Chemotherapy Toxicity in Older Adults With Cancer: A Prospective Multicenter Study. *Journal of Clinical Oncology*. 2011 Aug 30; 29(25):3457–3465. [PubMed: 21810685]
7. Extermann M, Boler I, Reich RR, Lyman GH, Brown RH, DeFelice J, et al. Predicting the risk of chemotherapy toxicity in older patients: The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. *Cancer*. 2012 Jul 1; 118(13):3377–3386. [PubMed: 22072065]
8. Hurria A, Cirincione CT, Muss HB, Kornblith AB, Barry W, Artz AS, et al. Implementing a geriatric assessment in cooperative group clinical cancer trials: CALGB 360401. *J. Clin. Oncol. American Society of Clinical Oncology*. 2011; 29(10):1290–1296.
9. Dobie SA, Baldwin L-M, Dominitz JA, Matthews B, Billingsley K, Barlow W. Completion of therapy by Medicare patients with stage III colon cancer. *J. Natl. Cancer Inst*. 2006 May 3; 98(9): 610–619. [PubMed: 16670386]
10. Soubeyran P, Fonck M, Blanc-Bisson C, Blanc J-F, Ceccaldi J, Mertens C, et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. *Journal of Clinical Oncology*. 2012 May 20; 30(15):1829–34. [PubMed: 22508806]
11. Hann D, Winter K, Jacobsen P. Measurement of depressive symptoms in cancer patients:: Evaluation of the center for epidemiological studies depression scale (Ces-d). *J Psychosom Res. Elsevier*. 1999; 46(5):437–443.
12. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch. Intern. Med*. 2003 Nov; 163(22):2716–2724. [PubMed: 14662625]
13. Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H. Validation of a short Orientation-Memory-Concentration Test of cognitive impairment. *Am J Psychiatry*. 1983 Jun; 140(6):734–739. [PubMed: 6846631]
14. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology*. 1982 Dec; 5(6):649–655. [PubMed: 7165009]
15. Katz S, Ford AB, Moskowitz R, Jackson B, Jaffe M. Studies of Illness in the Aged: The Index of ADL. *JAMA: The Journal of the American Medical Association*. 1963; 185:914–919. [PubMed: 14044222]
16. Lawton M, Brody E. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969; 9(3):179–186. [PubMed: 5349366]

17. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J. Gerontol. A Biol. Sci. Med. Sci.* 2001 Jun; 56(6):M366–M372. [PubMed: 11382797]
18. Piccirillo JF, Creech CM, Zequeira R, Anderson S, Johnston AS. Inclusion of comorbidity into oncology data registries. *J Registry Manage.* 1999; 26(2):66–70.
19. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann. Intern. Med.* 2006 Aug 15; 145(4):247–254. [PubMed: 16908915]
20. Frasci G, Lorusso V, Panza N, Comella P, Nicoletta G, Bianco A, et al. Gemcitabine plus vinorelbine versus vinorelbine alone in elderly patients with advanced non-small-cell lung cancer. *J. Clin. Oncol.* 2000 Jul; 18(13):2529–2536. [PubMed: 10893283]
21. Fairfield KM, Murray K, Lucas FL, Wierman HR, Earle CC, Trimble EL, et al. Completion of adjuvant chemotherapy and use of health services for older women with epithelial ovarian cancer. *Journal of Clinical Oncology.* 2011 Oct 10; 29(29):3921–3926. [PubMed: 21911719]
22. Freyer G, Geay J-F, Touzet S, Provencal J, Weber B, Jacquin J-P, et al. Comprehensive geriatric assessment predicts tolerance to chemotherapy and survival in elderly patients with advanced ovarian carcinoma: a GINECO study. *Ann. Oncol.* 2005 Nov; 16(11):1795–1800. [PubMed: 16093275]
23. Landi F, Liperoti R, Russo A, Giovannini S, Tosato M, Capoluongo E, et al. Sarcopenia as a risk factor for falls in elderly individuals: Results from the iLSIRENTE study. *Clin Nutr.* 2012 Mar 11. epub:1–7.
24. Hubbard RE, O'Mahony MS, Savva GM, Calver BL, Woodhouse KW. Inflammation and frailty measures in older people. *J. Cell. Mol. Med.* 2009 Sep; 13(9B):3103–3109. [PubMed: 19438806]
25. Krakauer JC, Franklin B, Kleerekoper M, Karlsson M, Levine JA. Body composition profiles derived from dual-energy X-ray absorptiometry, total body scan, and mortality. *Prev Cardiol.* 2004; 7(3):109–115. [PubMed: 15249762]
26. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *Journal of Clinical Epidemiology.* 1996 Dec; 49(12):1373–1379. [PubMed: 8970487]
27. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. *American Journal of Epidemiology.* 2007 Mar 15; 165(6):710–718. [PubMed: 17182981]
28. Kallogjeri D, Piccirillo JF, Spitznagel EL, Steyerberg EW. Comparison of Scoring Methods for ACE-27: Simpler Is Better. *J Geriatr Oncol.* 2012 Jul 1; 3(3):238–245. [PubMed: 22712031]
29. Repetto L, Fratino L, Audisio RA, Venturino A, Gianni W, Vercelli M, et al. Comprehensive geriatric assessment adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients: an Italian Group for Geriatric Oncology Study. *J. Clin. Oncol.* 2002 Jan 15; 20(2):494–502. [PubMed: 11786579]

Table 1**Baseline Demographics and Laboratory Values (N=65)**

Age (median, range)	73 (65–89)
Gender (frequency, percent)	
Female	38 (58.5%)
Male	27 (41.5%)
Race (frequency, percent)	
White	59 (90.8%)
Black	6 (9.2%)
Cancer Type	
Lymphoma	21 (32.3%)
Colorectal Cancer	27 (41.5%)
Breast	10 (15.4%)
Lung	7 (10.8%)
Living situation	
Single family home or apartment	61 (93.8%)
Long-term care or skilled nursing	2 (3.1%)
Retirement community/independent living facility	2 (3.1%)
Presence of a caregiver	52 (80%)
Type of caregiver	
Spouse/significant other	41/52 (78.8%)
Parent	1/52 (1.9%)
Adult child	9/52 (17.3%)
Friend	1/52 (1.9%)
Creatinine (mg/dl, median, range)	1.0 (0.46–2.3)
Albumin (mg/dl)	3.8 (2.2–5.4)
Hemoglobin (mg/dl)	12.0 (8.2–14.7)
Creatinine clearance estimated (ml/min) (median, range)	71.9 (29.9–142.3)
Chemotherapy intent	
Palliative	27 (41.5%)
Curative (adjuvant or definitive)	38 (58.5%)

Table 2**Geriatric Assessment Results**

Depression: CESD 4 (frequency, percent)	14 (21.5%)
Cognition: Short blessed test score (median, range)	2 (0–13)
Short blessed >9 (frequency, percent) *	3/63 * (4.8%)
Katz ADL score (median, range)	18 (11–18)
Dependence in ADLs (frequency, percent)	7 (10.8%)
Lawton IADL score (median, range)	25 (13–26)
Dependence in IADLs (frequency, percent)	25 (38.5%)
ECOG Performance status	
0	29 (44.6%)
1	26 (40%)
2	8 (12.3%)
3	2 (3.1%)
ACE comorbidity score	
None	11 (16.9%)
Mild	31 (47.7%)
Moderate	13 (20%)
Severe	10 (15.4%)
Body Mass Index	26.4 (15.0–40.2)
MNA score (median, range)	9 (1–11)
Number of medications (median, range)	6 (0–20)
On medications considered inappropriate in the elderly *	17/63 * (27.0%)
Falls in past month	9 (13.8%)

* Denominator reflects missing data

CESD, Center for Epidemiologic Studies-Depression; ADL, Activities of Daily Living; IADLs, Instrumental Activities of Daily Living; ECOG, Eastern Cooperative Oncology Group; ACE, Adult Comorbidity Evaluation-27; MNA, Mini-Nutritional Assessment.

Table 3**Multivariate Analysis of Factors Predictive of Completion of Chemotherapy**

	Univariate Analysis		Multivariate Analysis	
	OR(95% CI)	P	OR(95% CI)	P
Female Gender	0.46 (0.14–1.51)	0.20		
Race (White)	2.05 (0.22–18.97)	0.53		
Cancer				
Lymphoma	Ref	0.25		
Colorectal	0.81 (0.21–3.10)			
Breast	3.33 (0.34–32.96)			
Lung	0.25 (0.041–1.52)			
Living Situation				
Single Family	Ref	0.62		
Nursing	0.36 (0.021–6.08)			
Independent living	0.36 (0.021–6.08)			
Caregiver	0.73 (0.17–3.05)	0.66		
Falls	0.24 (0.06–1.04)	0.056		
Curative Intent	4.37 (1.33–14.33)	0.015	4.97 (1.21–18.81)	0.03
Depression	1.05 (0.28–3.93)	0.95		
ADL dependence	0.47 (0.093–2.35)	0.36		
IADL dependence	0.33 (0.10–1.06)	0.06	*	
Cognitive impairment	0.71 (0.06–8.46)	0.79		
ECOG PS 2–3	0.18 (0.04–0.77)	0.02	0.089 (0.015– 0.530)	0.008
Comorbidities (moderate-severe)	0.47 (0.15–1.49)	0.20		
Anemia	0.62 (0.17–2.21)	0.46		
Age	0.92 (0.84–1.01)	0.070		
Body Mass Index	1.06 (0.96–1.17)	0.23		
Creatinine Clearance (OR per ml/min)	1.027 (1.001–1.054)	0.04	1.03 (1.00–1.06)	0.04

* Not entered in multivariate model due to strong correlation with performance status

OR, odds ratio; CI, confidence intervals; ADL, activities of daily living; IADL, instrumental activities of daily living; ECOG PS, Eastern Cooperative Oncology Group Performance Status.

Table 4

Factors Predictive of Grade III/IV Non-Hematologic Toxicity

	Univariate		Multivariate	
	OR(95% CI)	P	OR (95% CI)	P
Female Gender	0.29 (0.094–0.90)	0.03 3	0.20 (0.01–0.75)	0.017
Race (White)	*	0.16		
Cancer				
Lymphoma	Ref	0.22		
Colorectal	0.43 (0.12–1.55)			
Breast	0.12 (0.013–1.13)			
Lung	0.92 (0.16–5.2)			
Living Situation				
Single Family	Ref	0.99		
Nursing	*			
Independent living	*			
Caregiver	1.023 (0.27–3.85)	0.97		
Falls	1.97 (0.47–8.37)	0.36		
Curative Intent	1.62 (0.52–5.10)	0.41		
Depression	2.92 (0.85–10.04)	0.09 0		
ADL dependence	1.78 (0.36–8.88)	0.48		
IADL dependence	1.62 (0.53–4.98)	0.40		
Cognitive impairment	*	0.55		
ECOG PS 2–3	2.64 (0.66–10.54)	0.17		
Comorbidities (moderate-severe)	4.40 (1.39–13.96)	0.01 2	6.13 (1.65–22.74)	0.007
Anemia	1.31 (0.37–4.61)	0.67		
Age	1.02 (0.94–1.11)	0.67		
Body Mass Index	1.09 (0.99–1.19)	0.07 4		
Creatinine Clearance (ml/min)	0.98 (0.96–1.00)	0.10		

* Not estimable due to 0 count of toxicity in the cell.

OR, odds ratio; CI, confidence intervals; ADL, activities of daily living; IADL, instrumental activities of daily living; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CrCl, creatinine clearance.

Table 5

Factors Associated with Increased Risk of Mortality

	Univariate		Multivariate	
	HR (95% CI)	p	HR (95% CI)	p
Female Gender	1.004 (0.42–2.39)	0.99		
Nonwhite race	*	0.14		
Cancer				
Lymphoma	Ref	0.09		
Colorectal	0.90 (0.33–2.40)			
Breast	*			
Lung	3.99 (1.23–12.92)			
Living Situation				
Single Family	Ref	0.59		
Nursing	2.048 (0.27–15.45)			
Independent	*			
Caregiver	1.61 (0.47–5.48)	0.45		
Falls	2.99 (1.06–8.42)	0.039	3.20 (1.13–9.11)	0.029
Intent (curative vs palliative)	0.16 (0.06–0.43)	<0.001	0.15 (0.06–0.42)	<0.001
Depression	1.28 (0.49–3.34)	0.62		
ADL dependence	0.38 (0.051–2.86)	0.35		
IADL dependence	2.00 (0.85–4.75)	0.11		
Cognitive impairment	0.83 (0.11–6.23)	0.86		
ECOG PS 2–3	1.74 (0.58–5.23)	0.32		
Comorbidities (moderate-severe)	1.70 (0.71–4.06)	0.23		
Anemia	0.40 (0.58–3.86)	0.70		
Age	1.06 (0.00–1.13)	0.099		
Body Mass Index	0.96 (0.89–1.04)	0.29		
Creatinine clearance	0.99 (0.97–1.01)	0.21		

* Not estimable due to 0 count of mortality in the cell

HR, Hazard ratio; CI, confidence intervals; ADL, activities of daily living; IADL, instrumental activities of daily living; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CrCl, creatinine clearance.