Short Communication

Comparison of an inflammation-based prognostic score (GPS) with performance status (ECOG) in patients receiving platinum-based chemotherapy for inoperable non-small-cell lung cancer

LM Forrest¹, DC McMillan*,¹, CS McArdle¹, WJ Angerson¹ and DJ Dunlop²

¹University Department of Surgery, Royal Infirmary, Glasgow G31 2ER, UK; ²Department of Medical Oncology, Royal Infirmary, Glasgow G31 2ER, UK

The value of an inflammation-based prognostic score (GPS) was compared with performance status (ECOG) in patients (n = 109) receiving platinum-based chemotherapy for inoperable non-small-cell lung cancer. On multivariate analysis with ECOG, white cell count and the GPS entered as covariates, only the GPS was a significant independent predictor of survival (HR 1.88, 95% CI 1.25–2.84, \( P = 0.002 \)).

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MATERIALS AND METHODS

Study design

Patients presenting with inoperable NSCLC (stages III and IV) to a single multidisciplinary oncology clinic in Glasgow Royal Infirmary between March 2000 and June 2003 were studied prospectively. All patients had cytologically or histologically confirmed disease and were staged on the basis of clinical findings, chest X-ray and, where appropriate, bronchoscopy, liver ultrasound, isotope bone scan and computerised tomography of the thorax, according to the American Thoracic Society TNM classification (Mountain, 1991).

Clinical stage, tumour type and performance status (Eastern Cooperative Oncology Group, ECOG) were recorded at the time of diagnosis. A blood sample was also obtained for the measurement of white cell count, albumin and C-reactive protein concentrations. Patients received between one and six cycles of platinum-based chemotherapy.

The study was approved by the Research Ethics Committee of Glasgow Royal Infirmary.

Methods

Blood parameters: Routine laboratory measurements of albumin and C-reactive protein concentration were carried out. The coefficient of variation for these methods, over the range of measurement, was less than 5% as established by routine quality control procedures.

The GPS was constructed as previously described (Forrest et al, 2003). Briefly, patients with both an elevated C-reactive protein (>10 mg l⁻¹) and hypoaalbuminaemia (<35 g l⁻¹) were allocated a score of 2. Patients in whom only one of these biochemical abnormalities was present were allocated a score of 1. Patients in whom neither of these abnormalities was present were allocated a score of 0.
Statistics

Univariate survival analysis was performed using the Kaplan–Meier method with the log-rank test. Multivariate survival analysis and calculation of hazard ratios (HR) were performed using Cox regression analysis. Deaths up to 31st October 2003 were included in the analysis. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

RESULTS

The characteristics of patients with inoperable NSCLC receiving platinum-based chemotherapy (n = 109) are shown in Table 1. The majority were male and over the age of 60 years. Approximately 50% had stage III disease, 90% had an ECOG performance status of 0–1, 75% had an elevated C-reactive protein and 10% had hypoalbuminaemia. The majority (68%) received cisplatin-based chemotherapy and the remainder carboplatin-based chemotherapy.

In total, 71 (65%) of patients died during the follow-up period. On univariate survival analysis, both white cell count and GPS were significant predictors of survival. Median survival times in the groups with an ECOG of 0, 1 and 2 were 16, 12 and 7 months, respectively, but were associated with wide confidence intervals and the difference in survival was not significant (Figure 1A). Median survival times in the groups with a GPS of 0, 1 and 2 were 17, 12 and 7 months respectively (P<0.01, Figure 1B).

On multivariate analysis with ECOG, white cell count and the GPS entered as covariates, only the GPS was a significant independent predictor of survival (HR 1.88, 95% CI 1.25–2.84, P = 0.002).

Table 1 Clinical characteristics and survival in patients with inoperable NSCLC receiving platinum-based chemotherapy: univariate survival analysis

| Patients | Survival (months) | P-value |
|----------|-------------------|---------|
| 109 (100%) | Median (95% CI) |         |
| Age      |                   |         |
| <60 years| 41 (38)           | 10.6 (3.8–17.3) | 0.681 |
| ≥60 years| 68 (62)           | 13.5 (11.2–15.9) |         |
| Sex      |                   |         |
| Male     | 63 (58)           | 15.1 (11.0–19.2) | 0.433 |
| Female   | 46 (42)           | 10.6 (10.1–11.1) |         |
| Stage    |                   |         |
| III      | 52 (47)           | 13.5 (9.1–18.0) | 0.337 |
| IV       | 57 (52)           | 12.2 (7.8–16.6) |         |
| Type     |                   |         |
| Squamous | 40 (37)           | 15.1 (7.9–22.4) | 0.451 |
| Adenocarcinoma | 46 (42) | 14.0 (9.5–18.6) |         |
| Other    | 23 (21)           | 11.7 (9.7–13.6) | 0.192 |
| Performance status (ECOG) |       |             |
| 0        | 29 (27)           | 16.0 (9.2–22.7) | 0.001 |
| 1        | 71 (65)           | 12.2 (9.9–14.5) |         |
| 2        | 9 (8)             | 7.1 (1.7–12.4)  | 0.405 |
| White cell count |       |             |
| <10 x10^9/l | 62 (56) | 16.6 (13.1–20.1) | 0.029 |
| ≥10 x10^9/l | 47 (44) | 11.7 (9.4–14.0) |         |
| GPS      |                   |         |
| 0        | 27 (25)           | 17.0 (14.0–19.9) | 0.005 |
| 1        | 69 (63)           | 12.1 (10.0–14.1) |         |
| 2        | 13 (12)           | 7.1 (4.9–9.2)   |         |

DISCUSSION

Conventionally, in patients with inoperable NSCLC, the decision whether or not to offer chemotherapy is primarily based on performance status. However, the assessment of performance status is subjective. For example, significant differences in the assessment of performance status have been reported between oncologists, nurses and patients, oncologists being the most optimistic in their assessment and patients the least (Ando et al, 2001). As a result there is continuing interest in the development of prognostic scores, which better reflect clinical outcome (Bennett and Ryall, 2000; Sloan et al, 2001).

In the present study, an inflammation-based prognostic score based on standard laboratory measurements, the GPS, appeared to be superior to performance status in predicting outcome following platinum-based chemotherapy. This may be in part because the assessment of performance status reflects functional status at a specific point in time. In contrast, the GPS, based as it is on the presence of an ongoing systemic inflammatory response and hypoalbuminaemia, predicts the progressive nutritional decline of...
the patient (McMillan et al., 2001; Scott et al., 2002). Indeed, it has long been recognised that progressive weight loss is associated with poor tolerance to chemotherapy (Chlebowski et al., 1996; Paesmans et al., 1997).

More recently, it has been reported that cytochrome P450 3A activity, the principal drug metabolising enzyme in a variety of chemotherapeutic agents, is compromised in advanced lung cancer patients with an elevated C-reactive protein concentration (Rivory et al., 2002; Slaviero et al., 2003). One might therefore postulate that the presence of a systemic inflammatory response would be associated with increased toxicity in patients receiving platinum-based chemotherapy. It was therefore of interest that 40% of patients with a GPS of 0 received six cycles platinum-based chemotherapy compared with only 9% of those with a GPS of 1 or 2 (P = 0.003, Fisher’s exact test). This suggests that the presence of a systemic inflammatory response may be an important factor in determining the ability of patients to tolerate platinum-based chemotherapy.

It is possible that in patients with inoperable non-small-lung cancer, an elevated C-reactive protein concentration might reflect intercurrent infection. If this were the case it might be expected that the increase in circulating C-reactive protein concentrations would be associated with a rise in the white cell count. However, in the present study, although the white cell count was significantly correlated with C-reactive protein concentrations, the magnitude of the relationship was small (r² = 0.6%). This would suggest that infection was not the main stimulus to the increased C-reactive protein concentrations.

The results of the present study suggest that the GPS offers additional prognostic information that may assist in the selection of appropriate patients with inoperable NSCLC for platinum-based chemotherapy.

REFERENCES

Ando M, Ando Y, Hasegawa Y, Shimokata K, Minami H, Nakai K, Ohno Y, Sakai S (2001) Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. Br J Cancer 85: 1634–1639

Bennett M, Ryall N (2000) Using the modified Barthel index to estimate survival in cancer patients in hospice: observational study. BMJ 321(7273): 1381–1382

Chlebowski RT, Palomares MR, Lillington L, Grosvenor M (1996) Recent implications of weight loss in lung cancer management. Nutrition 12(1 Suppl): S43–7

Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dunlop DJ (2003) Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. Br J Cancer 89: 1028–1030

Ikeda M, Natsugoe S, Ueno S, Baba M, Aikou T (2003) Significant host- and tumor-related factors for predicting prognosis in patients with esophageal carcinoma. Ann Surg 238: 197–202

Klastersky J, Paesmans M (2001) Response to chemotherapy, quality of life benefits and survival in advanced non-small cell lung cancer: review of literature results. Lung Cancer 34(Suppl 4): S95–S101

Mahmoud FA, Rivera NI (2002) The role of C-reactive protein as a prognostic indicator in advanced cancer. Curr Oncol Rep 4: 250–255

McMillan DC, Canna K, McArdle CS (2003) Systemic inflammatory response predicts survival following curative resection of colorectal cancer. Br J Surg 90: 215–219

McMillan DC, Watson WS, O’Gorman P, Preston T, Scott HR, McArdle CS (2001) Albumin concentrations are primarily determined by the body cell mass and the systemic inflammatory response in cancer patients with weight loss. Nutr Cancer 39: 210–213

Mountain CF (1991) A new international staging system for lung cancer. Chest 89(Suppl 4): 225s–233s

Numico G, Russo E, Merlano M (2001) Best supportive care in non-small cell lung cancer: is there a role for radiotherapy and chemotherapy? Lung Cancer 32: 213–226

O’Gorman P, McMillan DC, McArdle CS (2000) Prognostic factors in advanced gastrointestinal cancer patients with weight loss. Nutr Cancer 37: 36–40

Paesmans M, Sculier JP, Libert P, Bureau G, Dabouis G, Thiriaux J, Michel J, Van Cutsem O, Serysels R, Mommen P, Klastersky J (1997) Response to chemotherapy has predictive value for further survival of patients with advanced non-small cell lung cancer: 10 years experience of the European Lung Cancer Working Party. Eur J Cancer 33: 2326–2332

Rivory LP, Slaviero KA, Clarke SJ (2002) Hepatic cytochrome P450 3A drug metabolism is reduced in cancer patients who have an acute-phase response. Br J Cancer 87: 277–280

Scott HR, McMillan DC, Forrest LM, Brown DJF, McArdle CS, Milroy R (2002) The systemic inflammatory response, weight loss, performance status and survival in patients with inoperable non-small cell lung cancer. Br J Cancer 87: 264–267

Slaviero KA, Clarke SJ, Rivory LP (2003) Inflammatory response: an unrecognised source of variability in the pharmacokinetics and pharmacodynamics of cancer chemotherapy. Lancet Oncol 4: 224–232

Sloan JA, Loprinzi CL, Laurine JA, Novotny PV, Vargas-Chanes D, Krook JE, O’Connell MJ, Kugler JW, Tirona MT, Kardinal CG, Wiesendfeldt M, Tschetter K, Hatfield AK, Schaefer PL (2001) A simple stratification factor prognostic for survival in advanced cancer: the good/bad/uncertain index. J Clin Oncol 19: 3539–3546