Impact of treatment interruptions due to toxicity on outcome of patients with early stage (I/II) non-small-cell lung cancer (NSCLC) treated with hyperfractionated radiation therapy alone.

We investigated the effect of treatment interruptions due to high-grade (> or =3) toxicity on outcome of patients with early stage (I/II) non-small-cell lung cancer treated with hyperfractionated radiation therapy (Hfx RT). Of 116 patients treated with total tumour doses of 69.6 Gy, 1.2 Gy b.i.d. fractionation, 44 patients refused surgery while 72 patients were medically inoperable due to existing co-morbid states. Patients who were medically inoperable had worse KPS (P=0.0059) and more pronounced weight loss (P=0.0005). Among them, 12 patients experienced high-grade toxicity and 11 of them with either acute (n=6) or "consequential" late (n=5) high-grade toxicity requested interruption in the Hfx RT course (range, 12-25 days; median, 17 days). Superior survival (OS) was observed in patients who refused surgery when compared to those who were medically inoperable (P=0.0041), as well as superior local recurrence-free survival (LRFS) (P=0.011), but not different distant metastasis-free survival (P=0.14). Cause-specific survival (CSS) also favoured patients who refused surgery (P=0.004). Multivariate analysis showed independent influence of the reason for not undergoing surgery on OS (P=0.035), but not on LRFS (P=0.084) or CSS (P=0.068). Patients who refused surgery did not experience
high-grade toxicity (0/44), whereas 11 of 72 patients with medical inoperability and co-morbid states experienced high-grade toxicity and had treatment interruptions to manage toxicity (P=0.0064). Patients without treatment interruptions had significantly better OS (P=0.00000), LRFS (P=0.00000) and CSS (P=0.00000) than those with treatment interruptions. When corrected for treatment interruptions, the reason for not undergoing surgery independently influenced OS (P=0.040), but not LRFS (P=0.092) or CSS (P=0.068). In contrast to this, treatment interruption was independent prognosticator of all three endpoints used (P=0.00031, P=0.0075 and P=0.00033, respectively). When 11 patients with treatment interruptions were excluded, the reason for not undergoing surgery still affected OS (P=0.037) and CSS (P=0.039) but not LRFS (P=0.11). Multivariate analyses using OS, CSS and LRFS showed that the reason for not undergoing surgery affected OS (P=0.0436), but neither CSS (P=0.083) nor LRFS (P=0.080).