To assess the prognostic value of FDG PET/CT compared to the tumor markers S100B and melanoma inhibitory activity (MIA) in patients with high risk melanoma. Retrospective study in 125 consecutive patients with high risk melanoma that underwent FDG PET/CT for re-staging. Diagnostic accuracy and prognostic value was determined for FDG PET/CT as well as for S100B and MIA. As standard of reference, cytological, histological, PET/CT or MRI follow-up findings as well as clinical follow-up were used. Of 125 patients, FDG PET/CT was positive in 62 patients. 37 (29.6%) patients had elevated S100B (>100 pg/ml) and 24 (20.2%) had elevated MIA (>10 pg/ml) values. Overall specificities for FDG PET/CT, S100B and MIA were 96.8% (95% CI, 89.1% to 99.1%), 85.7% (75.0% to 92.3%), and 95.2% (86.9% to 98.4%), corresponding sensitivities were 96.8% (89.0% to 99.1%), 45.2% (33.4% to 55.5%), and 36.1% (25.2% to 48.6%), respectively. The negative predictive values (NPV) for PET/CT, S100B, and MIA were 96.8% (95% CI, 99.1%), 61.4% (50.9% to 70.9%), and 60.6% (50.8% to 69.7%). The positive predictive values (PPV) were 96.7% (95.0% to 99.1%), 75.7% (70.0% to 86.6%), and 88.0% (70.0% to 95.8%). Patients with elevated S100B- or MIA values or PET/CT positive findings showed a significantly (p<0.001 each, univariate Cox
regression models) higher risk of melanoma associated death which was increased 4.2-, 6.5- or 17.2-fold, respectively. PET/CT has a higher prognostic power in the assessment of cancer-associated mortality in melanoma patients compared with S100 and MIA.

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