PET-CT has Major Diagnostic Value in the Evaluation of Smoldering Multiple Myeloma

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Abstract

Background: Smoldering myeloma (SMM) is an indolent stage between monoclonal gammopathy of undetermined significance (MGUS) and active multiple myeloma (MM) defined as the absence of CRAB features and serum M protein ≥ 3 g/dl and/or ≥ 10% bone marrow plasma cells (BMPC).

Objective: The goal of this study was to determine the predictive value of PET-CT in patients with SMM and more specifically to determine if positive PET-CT was associated with a significant risk of progression to active disease in two years.

Methods: The Mayo Clinic Data Discovery and Query Database (DDQ) was utilized to identify patients with a diagnosis of SMM who underwent PET-CT. Positive PET-CT was defined as radiologist interpretation of increased uptake in one or more focal areas. The primary endpoint was progression to active MM within 2 years following PET-CT among patients with positive PET-CT and observed without treatment.

Results: 302 patients were identified as having SMM in whom a PET-CT was performed as part of the diagnostic evaluation. PET-CT was positive in 84 patients and negative in 118 patients. Of the 94 patients with positive PET-CT, 51 were diagnosed with MM and treated accordingly. Fourteen of these patients (27%) were upgraded to MM based on PET-CT findings alone. Thirty-three patients were observed without therapy. Of the 118 patients with negative PET-CT, 17 were upgraded to active disease based on other CT findings alone. Thirty patients were observed without therapy. Of the 118 patients with negative PET-CT, 15 were observed without therapy. Of the PET-CT positive group, 1938 (36%) progressed to active disease compared to 27/101 (27%) with negative PET-CT (p=0.0327) We then restricted analysis to PET-CT observed within 90 days of SMM diagnosis. Fourteen of 19 patients (74%) with positive PET-CT progressed within 2 years, compared to 12/40 patients (30%) with negative PET-CT (p=0.0027). Median time to progression (TTP) for patients with positive PET-CT was 17 months compared to 27 months in those with negative PET-CT (p=0.001). Of the 19 patients with positive PET-CT, 17 (94%) of 19 patients with underlying osteolysis had progression within 2 years compared to 86% (14) of patients without osteolysis.

Conclusions: Patients with positive PET-CT when observed without treatment have higher risk of progression to active disease. In comparison to those with negative PET-CT, underlying osteolysis seems to further increase this risk. This may be an underestimate as 12 patients who were treated based on PET-CT findings alone.

Background

• Risk of progression to active MM within 5 years of SMM diagnosis is 20%
• Current standard of care is observation without therapy until development of symptoms
• Early treatment as opposed to watchful waiting of patients with highest risk of progression has potential to improve quality of life and overall survival.

Methods

• Primary analysis: progression to active MM within 2 years of diagnosis in patients with positive vs negative PET-CT within 90 days after SMM diagnosis who were observed without therapy.
• Subgroup analysis: difference in probability of progression to MM based on presence or absence of underlying osteolysis in patients with positive PET-CT.
• Kaplan Meier curves and Wilcoxon were used for evaluation of differences of progression risk.
• Time-to-progression (TTP) was measured from the date of SMM diagnosis until progression to active disease.
• Data analysis was performed in JMP version 10.

Results

• In patients who underwent PET-CT within 90 days of SMM diagnosis, 74% with positive PET-CT progressed to MM within 2 years compared to 27% with negative PET-CT (p=0.0008).
• Median TTP in patients with positive PET-CT was 16 months vs 55 months in patients with negative PET-CT.
• Relative risk of progression to active MM in 2 years: 2.7 (95% CI 1.6-4.1).
• In patients with positive PET-CT, those with underlying osteolysis had increased incidence of progression (77% vs 66%, p=0.64).

Risk of progression

• PET-CT positivity is a strong prognostic indicator for progression of disease within two years of SMM diagnosis.
• Patients with a positive PET-CT and underlying osteolysis when observed without therapy have a high incidence of progression to active MM in two years.
• These results are likely an underestimate of the true risk as 14 patients were upgraded to MM and treated based solely on PET-CT findings.
• Our findings validate the recent International Myeloma Working Group recommendations that patients with a positive PET-CT and underlying osteolysis should be considered as active MM.

References

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