Elevated levels of serum midkine as a tumor marker in patients with digestive cancer.

H. Mouri, K. Ohtsubo, Y. Yamaguchi, H, Watanabe, and N. Sawabu

Midkine (MK) is one of a family of heparin-binding growth factors whose gene was identified in embrypnal carcinoma. MK messenger RNA (mRNA) is highly expressed in various tissues during the midgestation period of mouse embryogenesis, and it is considered to be involved in regulation of organogenesis. Increased MK mRNA and protein expression are exhibited in many human carcinomas such as gastric, pancreas, bile duct, colorectal, hepatocellular cancers as well as in Wilms' tumor and neuroblastoma. Serum level of MK is reportedly elevated in patients with esophageal cancer or neuroblastoma However, little is unknown about usefulness of determination of serum MK as a tumor marker in patients with digestive cancers. In the present study, we measured serum levels of MK in various digestive cancers and benign diseases, and evaluate its clinical significance as a tumor marker.

Serum levels of MK were measured by enzyme-linked immunosorbent assay (ELISA) using rabbit anti-human MK antibody as a first antibody, and biotinylated mouse anti-MK antibody as a second one in the sera from digestive malignant diseases (n=139) and benign diseases (n=87). The cut-off value of serum MK was set at 450pg/ml chiefly based on the ROC curve. The positive rate of MK in each cancer was as follows: 40% (14/35) in pancreatic cancer, 64% (23/36) in gastric cancer, 67% (16/24) in colorectal cancer, 38% (17/45) in hepatocellular cancer, and 71% (5/7) in bile duct cancer. Among patients with gastric or colorectal cancer, the positive rate of serum MK was relatively high and had no relation to the stage of cancer shown in Fig. High positivity of MK of gastric or colorectal cancer in stage I is worthy of notice. On the other hand, positivity of serum MK in benign digestive disease was as follows: 31% (5/16) in chronic hepatitis, 33% (4/12) in chronic pancreatitis, 16% (2/12) in acute pancreatitis, and 67% (6/9) in cholangitis., indicating that false positivity is high in inflammatory diseases.

In conclusion , serum MK level increased in a variety of digestive cancers, especially in gastric and colorectal cancer. These results suggest that determination of serum MK may be useful as an aid in initial screening of gastrointestinal cancers, although false positivity is high in inflammatory diseases.

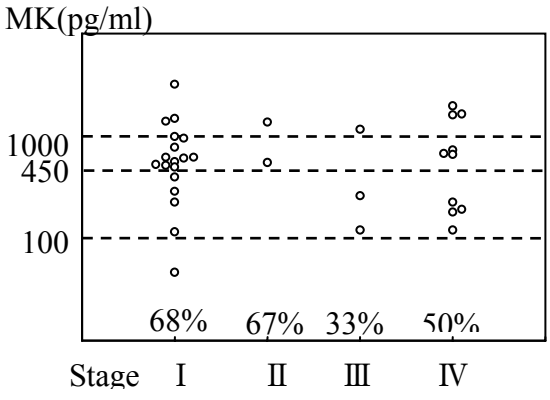

Fig. Relationships between serum MK levels and tumor stage in gastric cancer