

## Zollinger-Ellison Syndrome is Best Managed by Surveillance in Multiple Endocrine Neoplasia-1 and Surgery in Eligible Sporadic Cases

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**Background:** Zollinger-Ellison syndrome (ZES) management remains controversial because few institutions see sufficient patients to allow for comprehensive post-intervention analysis. We investigated surgical outcomes of ZES patients to determine the best approach to management of this population.

**Methods:** A retrospective chart review of 49 ZES patients seen at a tertiary care center since 1994 was performed. Cox proportional hazards modeling was used for survival comparisons between similar groups based on Multiple Endocrine Neoplasia-1 (MEN-1) and surgical status. Differences between variables were compared using the unpaired t-test and Fisher's exact test when appropriate.

**Results:** Of 49 ZES patients, 34 underwent surgery (9 with MEN-1). Compared to sporadic ZES patients, MEN-1-associated patients present earlier (34.9 vs. 45.7yrs;  $p < 0.05$ ), are diagnosed earlier (39.3 vs. 49.7yrs;  $p < 0.01$ ); yet, die at the same age (55.9 vs. 55.1yrs;  $p = 0.91$ ) with no MEN-1 deaths due to progressive disease (0% vs. 86%;  $p < 0.05$ ). Lymph node involvement at surgery likely increases risk of liver metastasis in the setting of the natural history of gastrinoma ( $p = 0.13$ ) and was significantly associated with lack of postoperative cure ( $p = 0.01$ ). Surgery decreased all-cause (HR 0.11 [0.2-0.6];  $p = 0.011$ ) and disease-related mortality (HR 0.14 [0.2-0.84];  $p = 0.032$ ) in sporadic, but not MEN-1, patients.

**Conclusions:** The presence of MEN-1 predicts earlier onset and diagnosis of ZES but a more benign clinical course rarely characterized by disease-related death in support of deferring surgery early on. However, sporadic ZES is associated with disease-related mortality that is reduced by early surgical intervention. Lymph node involvement at surgery likely increases the risk of liver metastases which, in almost all cases, occurred within 2 years of diagnosis. In addition, lymph node involvement decreased the likelihood of postoperative cure further supporting surgical intervention soon after diagnosis in eligible sporadic patients.

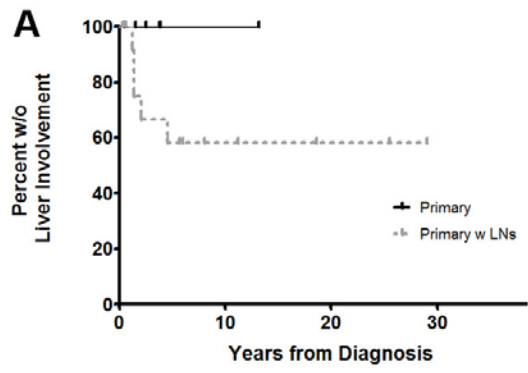


Figure 1: Development of Liver Metastases based on Lymph Node Involvement