Baretić M., Perkov D., Vuica P., Jakovčević A., Škegro M. (2018) ***Arterial calcium stimulation with hepatic venous sampling predicts the localization and size of the insulinoma as well as postoperative weight loss.*** **Scandinavian Journal of Gastroenterology, 53 (8). pp. 923-942. ISSN 0036-5521**

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Dear Editor,

We read the manuscript “Surgery in overweight patients with insulinoma: effects on weight loss” (1) with great interest and decided to share our experiences in treating patients with insulinoma, with regard to the prediction of tumor size and postoperative weight loss.The contemporary management of insulinoma is possible only with appropriate laboratory testing of hypoglycemic symptoms and exact preoperative localization. The management goal is to minimize unsuccessful pancreatic surgical resection (2). Our analysis aimed to investigate the relationship between tumor size and postoperative weight changes. We analyzed anamnestic data, laboratory values obtained during the 72-h fasting test and/or arterial calcium stimulation with hepatic venous sampling (ASVS) at patients with inconclusive noninvasive localization techniques, postoperatively established maximum diameter of the tumor size and observed postoperative weight loss.

Data from 11 patients (5 males, 6 females) who were diagnosed at the Department of Endocrinology, Internal Medicine Clinic, University Hospital Centre Zagreb, Croatia between 2007 and 2017 followed up for at least 6 months were retrospectively analyzed. Although noninvasive localization techniques (endoscopic US, CT, and MRI) were inconclusive, a diagnosis of endogenous hyperinsulinism was established in these patients. In some cases, there was a biochemically proven endogenous hyperinsulinism with indeterminate anatomy. In other cases, different localization techniques indicated different tumor sites. One patient exhibited tumor recurrence and was diagnosed with multiple endocrine neoplasia type 1. This patient was excluded from the analysis along with another patient who rejected surgery and was later treated with diazoxide. Descriptive statistics were used to describe the basic features of the study sample, and independent t-tests were used for between-group comparisons of the mean weight loss among patients with larger or smaller tumors. Correlation analyses were performed to test for the association between the glucose level during the 72-h fasting test and tumor size. Statistical analysis was performed at a confidence level of 95% ($\alpha = 0.05$).

The median patient age was 55 years (45–60) and median body mass index was 25.8 kg/m2 (21.3–40.3). Half of the patients reported weight gain before the diagnosis of insulinoma. Hypoglycemia was confirmed with the standard 72-h fasting test protocol. The mean of the lowest glucose level during the test was 1.7 mmol/L (1.0–2.1) without adequate insulin suppression.All patients underwent ASVS; standard pancreatic arteriography was performed, followed by selective catheterization of the gastroduodenal, splenic, and superior mesenteric arteries. An injection of calcium gluconate at a dose of 0.025 mEq/kg body weight was administered to every artery, and blood samples were obtained from the hepatic vein 10 min prior to the injection and at 30, 60, 90, and 120 s after the injection. The median peak insulin level was 410 mU/L (128–2195) during ASVS.

The peak insulin level following ASVS indicated the exact location of the tumor-feeding artery; it was the splenic artery in six patients, the gastroduodenal artery in three patients, and the superior mesenteric artery in two patients. Two patients underwent enucleation of the tumor from the body of the pancreas, and four underwent distal

pancreatectomy with splenectomy. One patient underwent pancreaticoduodenectomy, two patients underwent pancreatic head resection, and two patients underwent enucleation of the tumor from the uncinate process. There was no operative mortality, and all patients had benign tumors. One patient developed postoperative pancreatitis with pseudocyst formation, and one was diagnosed with hospital-acquired pneumonia. Complete symptom resolution was achieved in all cases. No patient had long-term endocrine pancreatic insufficiency, i.e., diabetes mellitus. The median tumor size was 1.7 cm (0.8–2.5). The median postoperative weight loss (shown as the percentage of the initial weight) in all patients was 10.5% at 6 ± 2 months and 13% at 18 ± 4 months.

A moderate positive correlation was found between the lowest glucose level during the 72-h fasting test and tumor size ($r = 0.45$) as well as between the peak insulin level during ASVS and tumor size ($r = 0.49$). Postoperatively, the patients were divided into two subgroups; those with tumors smaller than 1.5 cm [four patients with a median tumor size of 1.4 cm (range 0.8–1.5)] and those with tumors larger than 1.5 cm [eight patients with median tumor size of 1.8 cm (range 1.6–2.2)]. The cutoff value of the tumor size was 1.5 cm; this was similar to the mean tumor size of the insulinoma found our study as well in three previous larger studies with a total of 175 patients (3-5). Patients with tumors larger than 1.5 cm after 6 ± 2 and 18 ± 4 months lost 17 and 19% of their initial body weight, whereas those with tumors smaller than 1.5 cm lost 8% and 16% of their initial body weight, respectively. The between-group differences were statistically significant ($p = .05$).

In short, accurate preoperative localization and prediction of the size of the insulinoma are important for surgeons who wish to perform pancreatic-sparing surgery and preserve healthy pancreatic parenchyma (6). Our study found that the lowest glucose level during the 72-h fasting test and the peak insulin level during ASVS were related to the size of the insulinoma. Such information can help in planning the extent of the surgical procedure. Following the surgery, size of the tumor itself, predict short- and long-term weight loss.

References

1. Dai H, Xu Q, Hong X, et al. Surgery in overweight patients with insulinoma: effects on weight loss. Scand J Gastroenterol. 2017;52:1037–1041.
2. Ng HY, Pape A. Insulinoma: important in the differential diagnosis of persistent hypoglycaemia unrelated to diabetes. Med J Aust. 2018;208:157–158.
3. Grant CS. Surgical aspects of hyperinsulinemic hypoglycemia. Endocrinol Metab Clin North Am. 1999;28:533–554.
4. Doherty GM, Doppman JL, Shawker TH, et al. Results of a prospective strategy to diagnose, localize, and resect insulinomas. Surgery. 1991;110:989–996.
5. Thompson NW, Czako PF, Fritts LL, et al. Role of endoscopic ultrasonography in the localization of insulinomas and gastrinomas. Surgery. 1994;116:1131–1138.
6. Davi MV, Pia A, Guarnotta V, et al. The treatment of hyperinsulinemic hypoglycaemia in adults: an update. J Endocrinol Invest. 2017;40:9–20.