



The role of pancreatic enucleation in the minimally invasive era

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We appreciate the invitation to comment on the article “Minimally invasive versus open pancreatic enucleation. Systematic and meta-analysis of surgical outcomes” published in the *Journal of Surgical Oncology* (1). In this systematic review, the authors aimed to compare the surgical outcomes of minimally invasive pancreatic enucleation versus open pancreatic enucleation, with the primary outcome being the comparative rate of postoperative pancreatic fistula (POPF) between the two approaches. The authors concluded that minimally invasive surgery is not at higher risk of POPF.

Undoubtedly, there is ongoing interest on the feasibility and safety of pancreatic enucleation, as this procedure really spares pancreatic parenchyma. Pancreatic enucleation is indicated for the treatment of benign pancreatic tumors including insulinomas, small neuroendocrine tumors or benign cystic lesions, that do not require lymph node evaluation. Pancreatic enucleation is also indicated for the removal of solitary metastases derived from renal cell carcinoma (2,3). Enucleation is a really minimally invasive procedure as it enables the maximal preservation of pancreatic parenchyma, there is no need for dissection and reconstruction and it is associated with low blood loss. However, the incidence of pancreatic fistula remains high in this procedure. Preoperative imaging and intraoperative ultrasound assessment are crucial in ensuring that the tumor can be resected with negative resection margins and leaving the main pancreatic duct intact. Regarding pancreatic neuroendocrine tumors, the main indication of pancreatic enucleation concerns insulinomas (4-6). Apart from insulinomas, indications for simple enucleation

include small, less than 2 cm, non-functional pancreatic neuroendocrine tumors, that are distant from the pancreatic duct. However, there is still no consensus on the use of enucleation for the treatment of non-insulinoma pancreatic neuroendocrine tumors. The data regarding morbidity are conflicting. The most common complication following enucleation is development of a pancreatic fistula. POPF is associated with considerable morbidity and it occurs in up to 50% of patients.

Although the authors of the current manuscript aimed to compare the rate of pancreatic fistula between minimally invasive and open pancreatic enucleation, the main question is if the rate of pancreatic fistula after pancreatic enucleation is higher than the rate of POPF after the other pancreatic resections. Some authors report no difference in pancreatic fistula rates. On the other hand, there are studies that report a higher incidence of pancreatic fistula in the enucleation group. In addition, the severity of pancreatic fistula in case of enucleation tends to be lower than in the group undergoing formal resection. Furthermore, the rate of POPF seems to depend on the underlying pathology with the rate of clinical POPF being higher in patients with cystic neoplasms and an episode of acute pancreatitis (7). In addition, patients with genetic syndromes as Multiple Endocrine Neoplasia I and von Hippel Lindau have been reported to have higher incidence of POPF because of their underlying abnormal pancreatic parenchyma (8).

A matter of controversy still remains the comparative incidence of POPF between minimally invasive and open pancreatic enucleation. In fact, it would be anticipated that minimally invasive surgery led to lower rates of POPF in

comparison with open surgery. Since the rate of POPF is high, the aim of the minimally invasive surgery would be to result in lower rates of POPF. Is it feasible? It could be feasible through a better knowledge of anatomy, improvement of dexterity, surgical training outside the operating room (OR) through virtual reality training and mental practice.

Based on the above, the manuscript of Guerra *et al.* rather generates questions that provides answers. The authors come into a conclusion that has no clinically significant meaning, “minimally invasive surgery is not at higher risk of pancreatic fistula”. The methodology of the systematic review meta-analysis raises several issues. Literature data were limited. There were no randomized controlled trials. There was heterogeneity between the studies, that raises questions on the validity of the meta-analysis. The authors have excluded small case series and case reports. However, a large number of studies on pancreatic enucleation are small series, since pancreatic enucleation is often applied for rare diseases as pancreatic neuroendocrine tumors. Case reports often aim to present a surgical complication, thus the authors should have considered their inclusion in the systematic review. The systematic review that focuses on a question of safety needs to consider sources of literature that are usually excluded in systematic reviews of efficacy. This principle is well accepted in the field of drug safety and it should be also adopted in the field of surgical complications.

In conclusion, pancreatic fistula is a frequent complication of pancreatic enucleation. Pancreatic enucleation is a real minimally invasive procedure. The goal of minimally invasive approaches by laparoscopic or robotic assisted surgery should be the decrease of the rate of pancreatic fistula and all the other complications of the minimally invasive pancreatic enucleation. This goal could be achieved by improving the knowledge of anatomy, by improving dexterity, by standardization of the surgical procedure.

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