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**Case Report / Приказ болесника**

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**Radical antegrade modular pancreatectomy (RAMPS) – report of two cases and review of the literature**

Радикална антероградна модуларна панкреатоспленектомија (РАМПС) – приказ два случаја и преглед литературе

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## Radical antegrade modular pancreateosplenectomy (RAMPS) – report of two cases and review of the literature

Радикална антероградна модуларна панкреатоспленектомија (РАМПС) – приказ два случаја и преглед литературе

### SUMMARY

**Introduction** The radical antegrade modular pancreateosplenectomy (RAMPS) procedure was introduced as a modification of standard retrograde pancreateosplenectomy (SRPS). It was designed to establish a new surgical approach, with intension to increase possibility of achieving negative posterior (retroperitoneal) resection margin, as well as to provide complete N1-lymph node clearance.

**Outline of cases** We present two cases with diagnosed left-sided pancreatic tumors, who were surgically treated in our HPB department. Both patients underwent posterior RAMPS procedure. Postoperative course was uneventful in both patients.

**Conclusion** RAMPS is a safe procedure, because it provides complete vascular and bleeding control. It is superior procedure in oncologic terms comparing to SRPS, because it increases the rate of R0 resection, and provides larger number of lymph nodes harvested. Furthermore, RAMPS is associated with better overall survival.

**Keywords:** pancreatic carcinoma; left-sided pancreatic tumors; distal pancreatectomy; RAMPS

### САЖЕТАК

**Увод** Радикална антероградна модуларна панкреатоспленектомија (РАМПС) уведена је као модификација стандардне ретроградне панкреатоспленектомије (СРПС). Осмишљена је као нови хируршки приступ са намером да се повећа могућност за постизање негативне постериорне (ретроперитонеалне) ресекционе маргине као и са циљем комплетног уклањања свих N1 лимфних нодуса.

**Прикази болесника** Приказујемо два случаја болесника са туморима тела и репа панкреаса дијагностикованим мултидетектор компјутеризованом томографијом и магнетном резонанцом који су оперисани на нашем одељењу за хепато-билио-панкреатичну хирургију. Код оба пацијента урађен је задњи РАМПС. Постоперативни ток у оба пацијента протекао је без компликација.

**Закључак** РАМПС је безбедна хируршка процедура зато што омогућава потпуну контролу васкуларних елемената и потенцијалног крварења. РАМПС је онколошки супериорна техинка у односу на СРПС зато што резултира знатно већим стопама R0 ресекција и знатно већим бројем уклоњених лимфних нодуса. Такође, РАМПС је удружен са бољим дугорочним преживљавањем у односу на СРПС.

**Кључне речи:** карцином панкреаса; тумори тела и репа панкреаса; дистална панкреатектомија; РАМПС

### INTRODUCTION

Pancreatic cancer is one of the most lethal and aggressive tumors in human pathology, with median survival in untreated cases of 3-6 months, and a 5-year survival rate that ranges from 6 to 9% [1, 2]. Left-sided pancreatic cancer is often asymptomatic and more commonly diagnosed at an advanced stage. Surgical resection, often combined with chemo- and/or radiation therapy, is the only method which gives a chance of curing this disease. The first distal pancreatic resection was performed by Trendelenburg in 1882, and was standardized by Mayo in 1913 [3]. It is now well understood and widely accepted that R0 resection is the key factor in improvement of long-term survival [4]. Therefore, to increase the rates of R0

resections and reduce the recurrence rates, has always been a goal and a challenge for pancreatic surgeons. RAMPS procedure was designed as an answer to those tendencies in modern pancreatic surgery. It has been performed since 1999 and established by Strasberg as a novel technique in 2003 [5]. The three main principles of the operation are N1 lymph node dissection, modular setting of the posterior plan of dissection to improve the probability to achieve negative posterior resection margins, and right-to-left dissection for early and optimal vascular/bleeding control. The posterior plane of dissection can be directly on the left adrenal gland and Gerota fascia (anterior RAMPS) or can be posterior to the adrenal and Gerota fascia (posterior RAMPS), depending on the extent of penetration of the tumor on CT-scan (Figure 1). This new procedure and technique has shifted focus from pancreatic head tumors to less frequent but equally aggressive and even more sinister left-sided pancreatic tumors.

## REPORT OF CASES

### Patient 1

A 66-year-old female patient was admitted to our hospital for upper abdominal pain and discomfort, followed by a weight loss of around 10 kg for the last 2 months. Laboratory findings and tumor-marker serum levels (CEA, CA 19-9) were within the reference range. Abdominal multi-detector computed tomography (MDCT) and MRI detected a large tumor mass (65 × 35 × 45 mm) located in the tail of the pancreas with involvement of the greater curve of the stomach, spleen, and the left adrenal gland, after which a final decision for surgical resection was made (Figure 2).

The patient underwent posterior radical antegrade modular pancreatectomy (RAMPS) with wedge resection of the greater curve of the stomach (Figure 3).

It was the very first RAMPS performed at the Clinical Center of Serbia in Belgrade. The procedure lasted around 250 min and no blood transfusions were given. Histopathologic analysis revealed ductal invasive adenocarcinoma. The postoperative course was uneventful and a patient was discharged from the hospital after 11 days. Regular check-up were scheduled on every 3 months during the first postoperative year. The patient received adjuvant chemotherapy (Gemcitabin). One year after surgery, three liver metastases were detected on MDCT of the abdomen, two of which in the right liver lobe and one in the left.

Palliative chemotherapy treatment was started. Three months later multiple pulmonary metastases were detected with chest CT and three months after, patient died from hepatic failure in a terminal stage of malignant disease.

### **Patient 2**

The other patient was a 64-year-old female who was admitted after a large tumor (45 × 35 × 32 mm) was detected in the tail of the pancreas with abdominal MDCT and MRI. Imaging techniques showed extrapancreatic tumor propagation with infiltration of the splenic artery, splenic hilum, left adrenal gland and superior pole of the left kidney (Figure 4). Tumor-marker CA 19-9 serum level was elevated with a value of 383nmol/L. After a preoperative physical status assessment, a decision for a radical surgical procedure was made, and a patient underwent posterior RAMPS with left nephrectomy. Operative time was around 300 min and no blood transfusions were given. After histologic examination of the specimen by a pathologist, a diagnosis of pancreatic ductal invasive adenocarcinoma was established. Tumor stage was T3N1(3/27), and resection status was R1. The postoperative course was uneventful and patient was discharged from the hospital on the 12th postoperative day. Patient is currently receiving first course of adjuvant chemotherapy (Gemcitabine).

All procedures performed involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### **DISCUSSION**

Distal pancreatectomy is the standard surgical approach for left-sided pancreatic cancer. However, long-term survival of these patients remains unsatisfactory, with a median survival time of 10-28 months, and a 5-year overall survival of 6-30% [6, 7]. In recent years, new surgical approaches for resectable or borderline-resectable pancreatic head cancer, including the artery-first approach, superior mesenteric vein/portal vein resection and reconstruction, intraoperative radiotherapy and preoperative chemo-radiotherapy, have been increasingly combined with pancreaticoduodenectomy (PD). Despite the highly aggressive nature of the disease, and early regional lymph node metastasis, adenocarcinomas of the body and tail of the pancreas have attracted significantly less clinical attention. However, in 2003, Strasberg described a new distal pancreatectomy technique, termed radical antegrade modular

pancreatosplenectomy (RAMPS), to achieve negative posterior resection margins, and to remove the N1 lymph nodes completely [5]. In the RAMPS procedure, the lymph nodes along the superior and inferior borders of the left-sided pancreas (10, 11 and 18 according to JPS classification), the celiac lymph nodes (9) and nodes along the front and left side of superior mesenteric artery (14p, 14d) are considered N1 lymph nodes, and are completely removed. In the standard left-pancreatectomy, only lymph nodes 10, 11 and 18 are removed. Further, RAMPS is based on the anatomical architecture of the posterior pancreatic peritoneal fusion fascia (Gerota fascia, Treitz fascia and Toldt fascia). Using Kocher approaches, the inferior vena cava and left renal vein along the Treitz fascia level, behind the Gerota fascia, the left renal vein, the renal capsule, and the left adrenal gland, are separated to achieve a complete resection of the nerve fiber connective tissue of the tail, spleen, and lymph nodes, enhancing the rate of R0 resection of the posterior peritoneum.

In the past decade, the RAMPS procedure has been increasingly performed, particularly in Japan and Korea. Multiple studies from different centres have compared RAMPS to a standard retrograde pancreatosplenectomy (SRPS), evaluating postoperative complications, R0 resection rates and long-term survival after each type of procedure [7, 8]. A large meta-analysis from 2019 compared RAMPS to a standard retrograde pancreatosplenectomy [9]. Seven studies containing 474 patients have been enrolled in this meta-analysis, including 168 patients who underwent RAMPS and 306 patients who underwent SRPS. Three were prospective and four were retrospective studies. The studies were conducted in five countries, China, Italy, Japan, Korea and USA. The pooled analysis showed that RAMPS patients had better overall survival (OS) compared to a SRPS group of patients. This, however, did not apply to disease-free survival (DFS) which did not improve in RAMPS patient group. Further, blood loss in the RAMPS group was significantly less than in SRPS group, rendering the importance of early vascular control of major blood vessels in RAMPS technique. Regarding the number of harvested lymph nodes, significantly more lymph nodes were harvested in RAMPS than in SRPS group. It is calculated that at least 21 lymph nodes should be removed and analyzed, to ensure a reliable assessment of the nodal status. Although, it has been showed that extended lymphadenectomy does not improve survival, more harvested lymph nodes may result in more accurate node and tumor staging, thus more precisely identify the group of patients who could benefit from postoperative chemotherapy. Recurrence rate in RAMPS group is significantly lower than in SRPS patients group. Since RAMPS is using a so-called “no-touch isolation technique” (NTIT), it is fair to assume that

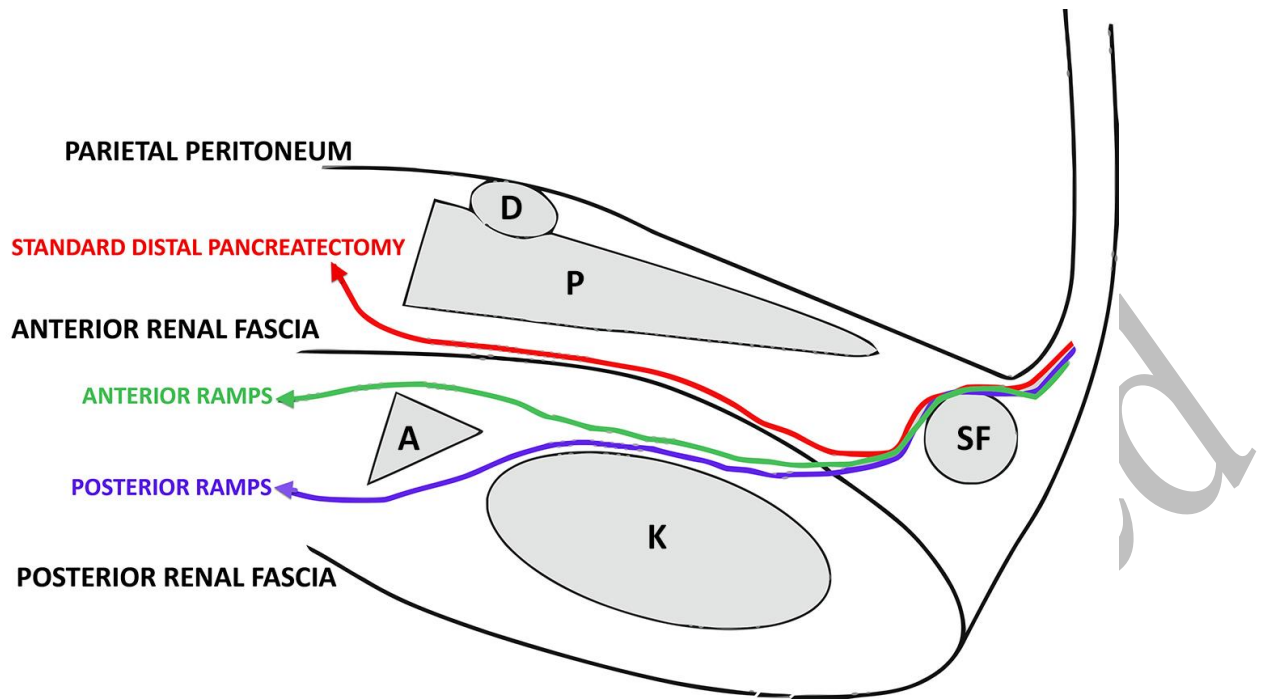
this might result in the reduction of distant tumor cells spread. Surprisingly, this meta-analysis, in contrast to that of Cao et al from 2017, did not show any significant difference in R0 rate between the RAMPS and SRPS patients group [10]. Meta-analysis and systemic review by Cao et al included six retrospective cohort studies with a total of 378 patients. RAMPS was done in 152 patients and 226 patients underwent standard procedure. In this study R0 resection rates were significantly higher in the RAMPS group. However, no statistically significant difference between groups was detected with respect to the recurrence rate. Further, there was no significant difference regarding the OS rate between the two groups of patients, which also applies to the comparison of DFS between groups. As expected, the number of lymph nodes harvested in RAMPS patients was significantly higher than in those in the standard group. Despite of higher multivisceral resection rate in RAMPS patients, incidence of postoperative complications did not increase. Also, there was no significant difference in the length of hospital stay, when comparing two groups of patients [10]. RAMPS procedures required greater technical skills, as well as longer operative times, but not in the terms of statistical significance, RAMPS patient group exhibited a tendency towards improvement of a median survival but no improvement in recurrence rates. Also, DFS rates were similar in two groups. It should be stated here that laparoscopic or robotic RAMPS have also been performed with satisfactory oncological results and survival outcomes [11, 12]. However, this approach should be limited to highly selective cases. Lee proposed Yonsei criteria by which only the following groups of patients should be treated with minimally invasive RAMPS: a).tumor confined to the pancreas, b) intact fascia layer between the distal pancreas and the left adrenal gland and kidney, and c) tumor is localized at least 1–2 cm from the celiac axis [11].

RAMPS is a safe surgical procedure providing superior vascular and bleeding control comparing to SRPS. RAMPS is also a superior procedure in oncologic terms comparing to SRPS, since it increases the rate of R0 resections, and provides larger number of lymph nodes harvested. Further, RAMPS does not increase the rates of postoperative complications. Also, there seem to be an improvement in overall survival with RAMPS technique. However, further randomized controlled clinical trials of high quality are needed to draw a more solid conclusions regarding long-term survival benefit.

**Conflict of interest:** None declared.

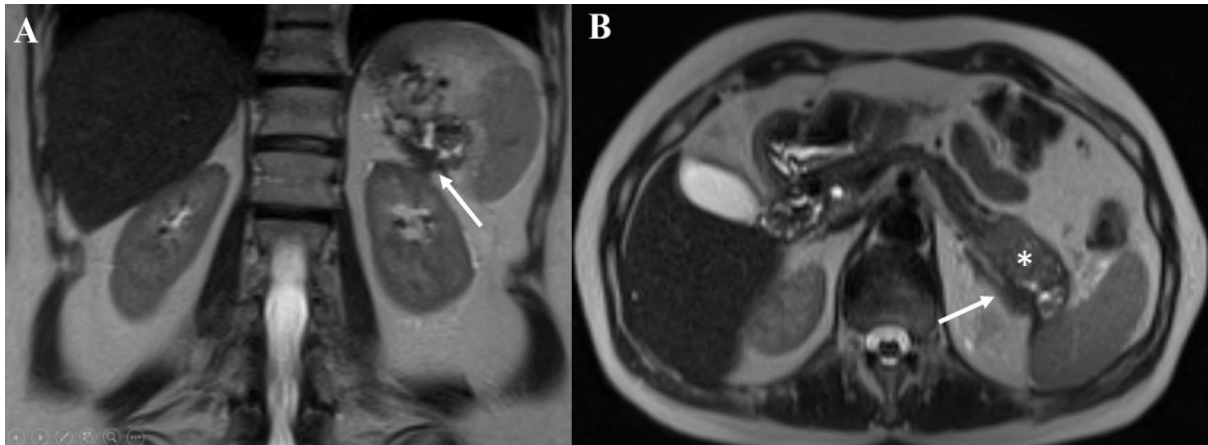
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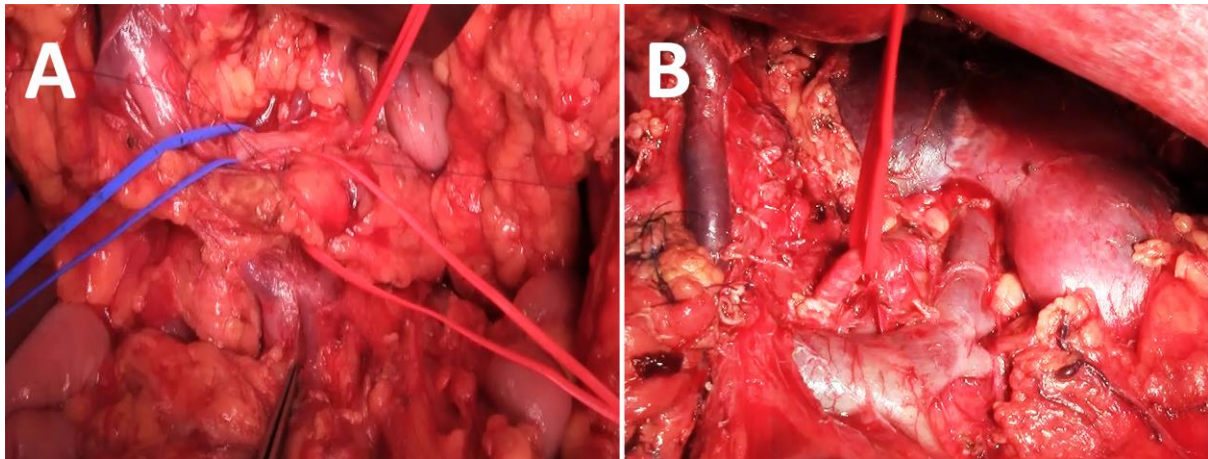


**Figure 1.** Left retroperitoneum plane of posterior margin of the RAMPS procedure; A – left adrenal gland; SF – splenic flexure of colon; D – fourth part of duodenum; K – left kidney; P – pancreas



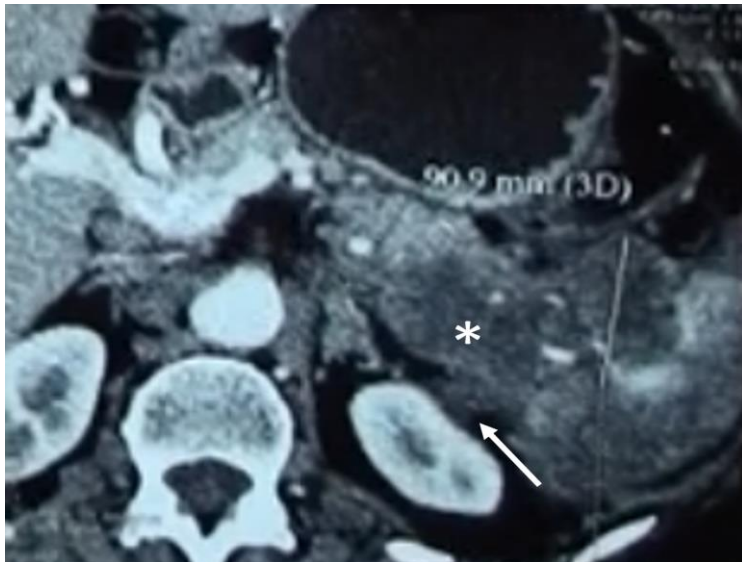


**Figure 2.** Coronal T2-weighted MR image (A) shows propagation of the pancreatic tail tumor in perirenal fat plane with infiltration of the renal capsule (arrow); axial T2-weighted MR image in the same patient (B) shows infiltration of left adrenal gland (arrow); pancreatic tail tumor shown on B (asterisk)



**Figure 3.** A) Early vascular control; B) retroperitoneal plane after removal of the specimen

Paper accepted



**Figure 4.** Coronal reformatted CT image in late arterial phase shows large tumor (asterisk) with infiltration of the perirenal fat on the left adrenal capsule (arrow); also note infiltration of the hilus of the spleen with consequent infarction of the splenic parenchyma

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