Section: General Surgery

Case Series

RAMPS FOR DISTAL PANCREATIC TUMOURS: OUR EXPERIENCE

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ABSTRACT

Background: Distal pancreatic cancers are relatively rare carcinomas and are associated with high mortality in view of advanced stage at presentation. In 2003, Strasberg and colleagues introduced radical antegrade modular pancreatico-splenectomy (RAMPS) with the philosophy of resecting the tumours with adequate tangential margin to improve survival of resectable distal pancreatic cancer compared to those treated with classical distal pancreatico-splenectomy. Recent advances include laparoscopic or robotic RAMPS including artery first approaches to achieve better outcome. We hereby report our experience with four cases of open RAMPS done for pancreatic body-tail tumours.

Materials and Methods: This retrospective study includes patient data from prospectively maintained database from the Department of General Surgery, Pathology and Radiotherapy and Medical Oncology Departments from a tertiary center of West Bengal from 2017-2023. Patients with pancreatic body-tail tumours who fulfilled the Yonsei criteria underwent radical antegrade modular pancreatico splenectomy as described by Strasberg and colleagues. Intraoperative details, postoperative complications, and detailed histopathology reports were recorded. Adjuvant therapy were administered with Gemcitabine and Capecitabine followed by external beam radiation therapy. Patients were followed up to observe RFS and OS.

Results: Three patients were male and one patient was female. Median age of the patients was 61 years with a range of 28 years to 67 years. Mean CA 19.9 level was 630 ± 531.79 IU/ml. All the patients had tumours located in the body and tail region of the pancreas and the mean tumour size was 10.25 ± 3.4 cm. On histopathology examination three turned out to be moderately differentiated adenocarcinoma and one case was diagnosed as well differentiated solid papillary epithelial neoplasm. For pancreatic adenocarcinoma cases mean RFS was 14 ± 5.29 months. Two patients had local recurrence and one patient developed liver metastases and received further chemotherapy with FOLFIRI after recurrence. Mean OS was 21 ± 11 months.

Conclusion: RAMPS is a safe technique for resection of pancreatic body-tail tumours without added morbidities and might offer survival benefit over conventional distal pancreatico-splenectomy as this technique is associated with improved R0 resection.

Keywords: Distal pancreatectomy, RAMPS, pancreatic body tail tumours, pancreatic resection.

INTRODUCTION

Distal pancreatic cancers are relatively rare carcinomas and are associated with high mortality in view of advanced stage at presentation as they are mostly manifested with vague symptoms. The cumulative risk of incidence of pancreatic cancer is 1 in 519 in lifetime as reported in a recent analysis from cancer registries in India.[1] Historical data from the United States reported an age-adjusted incidence rate of pancreatic cancer of 7.2 per 100000 population among which 5.6 cases were arising from the pancreatic head region and 1.6 cases from the pancreatic body-tail region. For the population above 70 years, the incidences increased sharply to 35.9 per 100000 for pancreatic head cancers and 9 per 100000 for pancreatic body-tail cancers, thus making the distal pancreatic cancers a rare entity and only 20% of them present as loco-regional disease with 3-year overall survival of approximately 5%.[2] Conventional distal pancreatico-splenectomy is carried out for the resectable distal pancreatic cancers as introduced by Trendelenburg and later standardized by Mayo. This comprises of left to right dissection and late ligation of splenic vasculature. Cuschieri introduced laparoscopic resection methods for distal pancreatic tumours in 1994.[3] However, the survival outcome for resectable pancreatic body tail tumour remained dismal. In 2003, Strasberg and colleagues introduced radical antegrade modular pancreatico-splenectomy (RAMPS) with the philosophy of resecting the tumours with adequate tangential margin to achieve R0 resection and extended lymphadenectomy for appropriate staging and provision of adjuvant treatment to prolong survival.[4] RAMPS is described as anterior or posterior depending on the depth of the posterior extent of the resection in respect of the left adrenal gland depending on the tumour infiltration of the same.[4-5] With the introduction of the artery first approach for resecting pancreatic head cancers to achieve complete resection (R0) around the major vessels to improve oncological outcomes the same principles were applied to the resection of distal pancreatic tumours as well thus introducing artery first RAMPS. Recent advances include laparoscopic or robotic RAMPS including artery first approach to achieve better outcome.[6-8] We hereby report our experience with RAMPS done for three cases of pancreatic adenocarcinoma and a case of solid and papillary epithelial neoplasm of the pancreas.

MATERIALS AND METHODS

This retrospective study includes patient data from prospectively maintained database from the Department of General Surgery, Pathology and Radiotherapy and Medical Oncology Departments from a tertiary center of West Bengal from 2017-2021. Patients with pancreatic body-tail tumours who fulfilled the Yonsei criteria were included in this study; stating so, the patients with tumours confined to the body or tail of the pancreas and which were located at least 1 cm from the celiac axis were selected for RAMPS to obviate the need of any major vascular resection (9).

After a clinical diagnosis was made with appropriate imaging i.e. a pancreatic protocol MDCT of the abdomen including thorax and pelvis or an abdominal MRI the patients were selected for a RAMPS procedure as per the inclusion criteria. Further investigations including CA 19-9 and CEA level, CBC, LFT, RFT, Coagulation profile, EKG, Chest X Ray and 2D Echocardiography were carried out. Patient's demographics and comorbidities were also recorded.

We followed the surgical technique as described by Strasberg (4). In brief, the neck of the pancreas was approached through the lesser sac from above and following the third part of the duodenum and inferior border of the pancreas to the portal vein from below. Lymph nodes along the common hepatic artery, hepatic artery proper and the nodes anterior to the portal vein were mobilized at this stage. After isolating the pancreatic neck from above and below the tunnel of Love was created and pancreatic neck was divided with either a surgical stapler or with harmonic scalpel keeping no less than 1 mm of healthy tissue from the tumour margin. Pancreatic duct and the cut end of the remnant gland were oversewn with 3-0 polydioxanone sutures. Next, the celiac lymph nodes were cleared and the origin of splenic artery was isolated and transfixed and divided. Ligation of left gastric artery was optional and depended on the presence or absence of origin of aberrant left hepatic artery from the left gastric artery. Splenic vein was isolated and divided next. The dissection then proceeded vertically in a sagittal plane to reach and dissect the lymph nodes to the anterior and to the left of the superior mesenteric artery and from the aorta between the origins of the CA and SMA. For anterior RAMPS dissection now deflected laterally in front of the adrenal vein, adrenal gland and anterior surface of the upper part of left kidney after lifting the Gerota's fascia. The inferior mesenteric vein was also ligated at the inferior border of the pancreas and the specimen was removed after division of the lienorenal ligament. For one patient (Case-4), posterior RAMPS was carried out as there was intraoperative suspicion of left adrenal invasion which was not evident on pre-operative imaging. For posterior RAMPS the dissection to the left side of aorta was deepened onto the diaphragm. The dissection was carried onto the diaphragm and the retroperitoneal muscle layers behind the adrenal on the body wall. The adrenal vein was divided flush with the renal vein and the adrenal gland was removed with the specimen. Left renal vein formed the inferior border of the dissection margin.

Intraoperative variables were noted which included operative duration, estimated blood loss, diameter of the pancreatic ducts at the cut margin, operative variant i.e. anterior vs posterior RAMPS, and ICU

and hospital stay. Postoperative complications and detailed histopathology reports were also recorded. Adjuvant therapy were administered with Gemcitabine and Capecitabine followed by external beam radiation therapy. Patients were followed up every 2 weeks for the first month and 3 months thereafter. Triphasic CECT abdomen was performed at six months' intervals or earlier if deemed essential as per the clinical presentation. RFS and OS were noted.

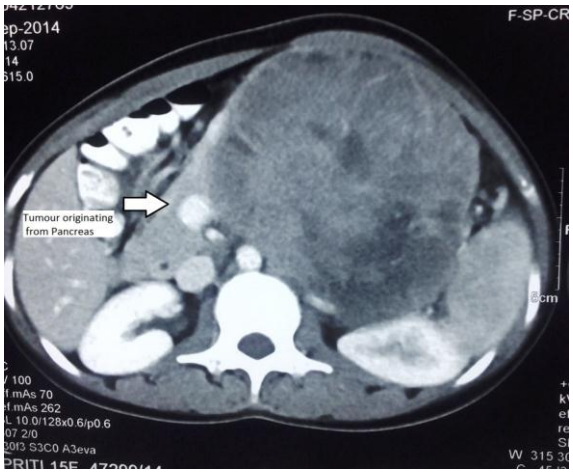
RESULTS

Three patients were male and one patient was female. Median age of the patients was 61 years with a range of 28 years to 67 years. All the male patients were smokers and two of them were recently diagnosed diabetic. Mean CEA level was 6.7 ± 4.43 IU/ml and mean CA 19.9 level was 630 ± 531.79 IU/ml. All the patients had tumours located in the body and tail region of the pancreas and the mean tumour size was 10.25 ± 3.4 cm. Mean operative duration was 225 ± 16 min and mean blood loss was 475 ± 65 ml. On histopathology examination three turned out to be moderately differentiated adenocarcinoma and one case was diagnosed as well differentiated solid papillary epithelial neoplasm. Pancreatic adenocarcinoma cases were further analysed. All resection margins were negative for tumour involvement and two patients had loco-regional lymph nodal involvement. All the patients were subjected to adjuvant chemotherapy with Gemcitabine and Capecitabine followed by external beam radiation therapy. Mean RFS was 14 ± 5.29 months. Two patients had local recurrence and one patient developed liver metastases and received further chemotherapy with FOLFIRI after recurrence. One patient was lost to follow up. Mean OS was 21 ± 11 months.

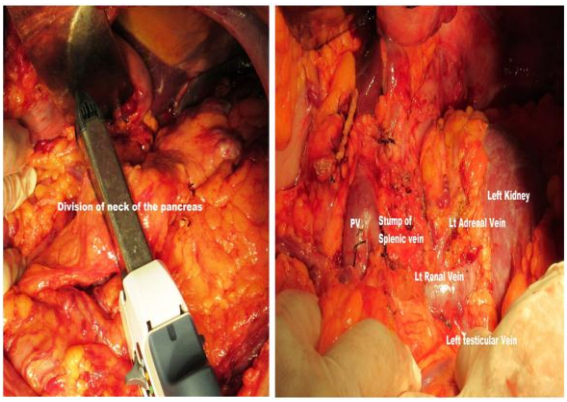
Table 1: Details of the patients are as below

	Case-1	**Case-2**	**Case-3**	**Case-4**
Age (yrs)	67	28	63	59
Gender	M	F	M	M
BMI kg/m2	21	19	23	20
Smoking status	Smoker	No	Smoker	Smoker
Diabetes status	Diabetic	No	Diabetic	No
Pre op CEA IU/ml	5.6	2.2	6.2	12.8
Pre op CA 19-9 IU/ml	482	40	678	1320
Tumour location body/tail	Body and tail	Body and tail	Body and tail	Body and tail with left adrenal involvement
Diameter of MPD at the cut surface (mm)	3	2	3.5	2.5
Type of RAMPS	Anterior	Anterior	Anterior	Posterior
Operative duration (min)	215	230	210	245
Estimated blood loss (ml)	400	500	550	450
Blood transfusion (units)	1	2	2	2
CR-POPF (yes; if yes grade/no)	no	A	no	B
CD grade complication	0	1	2	1
Chyle leak (yes/no)	No	No	No	No
Tumour size (cm)	9	15	10	7
Histology	Adenocarcinoma	SPEN	Adenocarcinoma	Adenocarcinoma
Tumour differentiation	Moderately differentiated	Well differentiated	Moderately differentiated	Moderately differentiated
LVI	Yes	No	Yes	Yes
PNI	No	No	Yes	No
LN ratio	0/8	0/4	1/9	2/12
R0/R1 resection	R0	R0	R0	R0
Adjuvant therapy	Yes	No	Yes	Yes
RFS (mo)	20	60	12	10
OS (mo)	32	60	21	Lost to F.U.

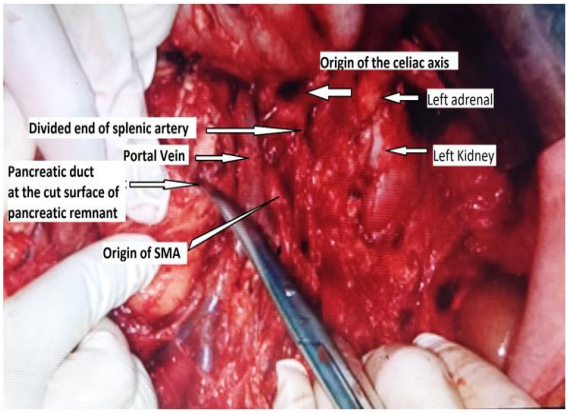
a) MDCT abdomen showing homogeneous lesion involving the pancreatic body-tail region with contrast enhancement in the parenchymal phase image; Case 1



b) MDCT abdomen showing large heterogeneous solid-cystic lesion involving the pancreatic body-tail region with variegated appearance in the parenchymal phase image; Case 2

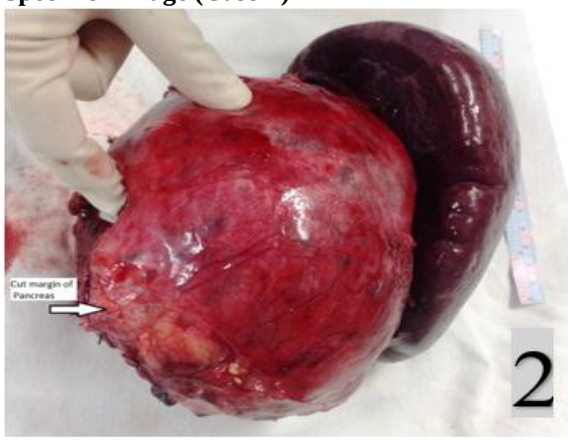


Operative images: Case 1: Division of pancreatic neck before mobilization of the tumour; Operative field after removal of the specimen



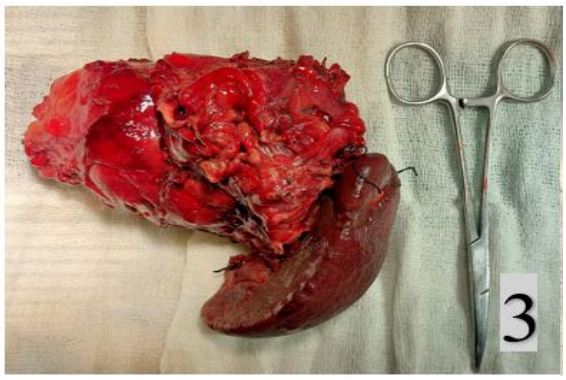
Operative images: Case 3: Operative field after removal of the specimen

Specimen image (Case-1)

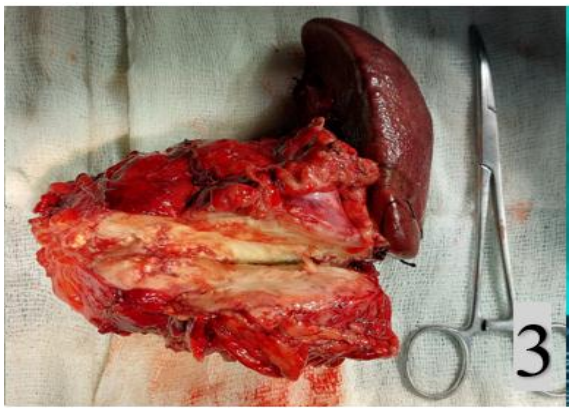


Specimen image (Case-2)

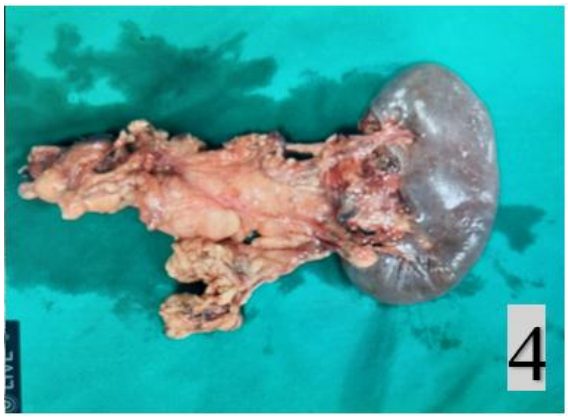
Specimen image (Case-2)



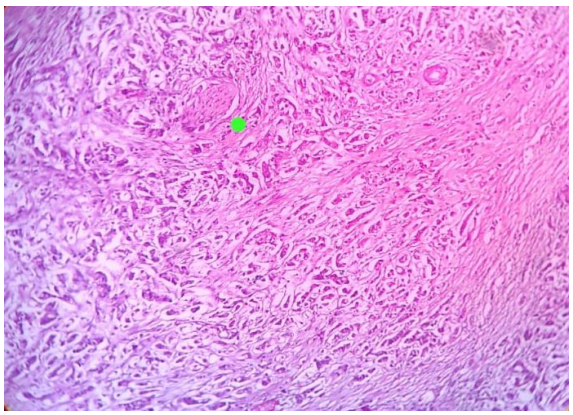
Specimen image (Case-3)



Specimen image (Case-3)



Specimen image (Case-4)



Case 3: Microphotograph of pancreatic ductal adenocarcinoma, H&E 400 X. The area marked with green dot shows perineural invasion

DISCUSSION

This is known that conventional technique of distal pancreatico-splenectomy is associated with poor 5-year survival which ranges from 0-20% of the cases.[10-11] This is also known that mortality results from high incidences of local and systemic recurrence. The risk factors for recurrence are increased pre-operative CA19.9 levels, large tumour size, poor tumour differentiation, lymph nodal involvement including involvement of non peripancreatic lymph nodes namely the stations 8-9, 12, 14-16, macrovascular involvement, extranodal visceral involvement and tumour infiltration of retroperitoneal fatty tissue, presence of LVI and PNI, Type of surgical intervention RAMPS versus standard DPS, resection status R0/R1, and no adjuvant chemoradiotherapy.[11-14] Only patients with negative resection margins and adequate lymphadenectomy without any residual disease are seen to enjoy long term disease free life.[2,15] Another important determinant for longer survival is the treatment with adjuvant chemotherapy or chemoradiotherapy.[16-18]

Proponents of this technique argue that RAMPS is associated with increased chances of a R0 resection and might have survival benefit compared to a conventional distal pancreatico-splenectomy.[19-21] However, systematic review and meta-analyses performed so far indicate similar outcomes of the distal pancreatico-splenectomy and RAMPS in terms of survival outcome.

Park and colleagues in their study demonstrated that RAMPS procedure facilitates the retrieval of a greater number lymph nodes than patients undergoing conventional distal pancreatico-splenectomy [median 14 (5–52) vs. 9 (1–36), $p < 0.05$]. Poor overall survival (OS) followed a conventional distal pancreatico-splenectomy, no adjuvant chemoradiation therapy (CRT), and non-curative resection on univariate analysis. Patients not receiving any adjuvant CRT and resection margin status were the determinants for worse OS on multivariate analysis.[18]

Another study by Jonathan B Mitchem and colleagues studied the long term outcome of forty - seven patients with adenocarcinoma of the pancreatic body-tail region who underwent either anterior or posterior RAMPS along with mutivisceral resection in a significant number of cases. The R0 rate was 81%. Mean lymph node count was 18. 5-year overall actuarial survival was 35.5% and the actual 5-year survival of 23 patients (with follow up of more than 60 months) was 30.4%.[22] It is also reviewed that the best way to reach to a conclusion about the superiority of RAMPS over standard DPS in terms of overall survival at least 556 patients with 228 patients in each arms need to be analysed in a RCT which is difficult to perform in view of the rarity of the tumours and the evolving surgical procedures in vogue.[22]

A study involving patients treated for pancreatic body-tail cancers at two large volume centers one from the USA and one from China, undergoing 193 DPS and 253 RAMPS revealed that DPS was associated with higher rates of R0 resection (94.3% vs. 88.9%, P=0.013) and higher numbers of lymph node harvestment (18 vs. 12, P<0.001) but was also associated with higher median estimated blood loss (500 vs. 300 cc, P<0.001). Postoperative complication rates such as CR-POPF and postoperative haemorrhage were similar in both the groups. RFS and OS were also similar in both the groups over a median follow up of 24.3 months with 5-yr OS approximately 20%.[11]

A systematic review and meta-analysis by Feng Cao and colleagues studied 378 patients with pancreatic adenocarcinoma and compared the outcome of 152 cases of RAMPS procedures with 226 cases of standard distal pancreatico-splenectomy and noticed that RAMPS resulted in higher R0 resection rates [Odds Ratio (OR) 95% confidence interval (CI), 2.19 (1.16 ~ 4.13); P = 0.02] and higher numbers of retrieved lymph nodes [weighted mean difference (WMD) 95% CI, 7.06 (4.52 ~ 9.60); P < 0.01] suggesting a superior oncological outcome of RAMPS compared with the standard procedure. However, the recurrence rates [OR 95% CI, 0.66 (0.40 ~ 1.09); P = 0.10], OS [Hazard ratio (HR) 95% CI, 0.65 (0.42 ~ 1.00); P = 0.05] and DFS [HR 95% CI, 1.02 (0.62 ~ 1.68); P = 0.93] were similar in the two groups. Operating time, blood loss, postoperative complications and hospital stay were also comparable.[23]

Another systematic review and meta-analysis by Zhen Huo and colleagues incorporating 474 patients compared the outcomes of RAMPS and DPS and found that significantly more lymph nodes were harvested in the RAMPS group compared with that in the DPS group (WMD=4.74, 95% CI: 0.36–9.12, P=0.034). Moreover, the recurrence rate (RR=0.8, 95% CI: 0.66–0.98, P=0.028) and blood loss (WMD=–153.19 ml, 95% CI: –303.95 to –2.42, P=0.046) were significantly low in the RAMPS group. Although the RAMPS group had a better overall survival (OS) compared with the DPS group (HR=0.65, 95% CI: 0.43–0.99, P=0.046; I2=41.8%, P=0.143) the differences were not statistically significant.[24]

The largest systematic review and meta-analysis done so far by Jun Watanabe and colleagues included thirteen cohort studies and analysed the results of RAMPS (770) versus DPS (871) and identified statistically significant advantages of RAMPS in terms of disease- free survival (hazard ratio [HR] 0.62, 95% confidence interval [CI] = 0.42- 0.91), but it had little effect on overall survival (HR 0.92, 95% CI = 0.79- 1.09) and recurrence- free survival (HR 0.72, 95% CI = 0.37- 1.38).[25]

In a prospective study by Hanyu Zhang and colleagues, outcome of 25 lap-RAMPS cases were compared with 23 open-RAMPS. There was no difference in R0 resection, margin status, number of lymph nodes retrieved, DFS (18.11 m vs 20.00 m, P = 0.999) and OS (24.53 m vs 28.73 m, P = 0.633) in the two RAMPS groups.[26]

In a study by Nan Niu and colleagues from China results of Laparoscopic RAMPS (n=50) were compared with Laparoscopic DPS (n=59) which suggested the oncological superiority of LRAMPS in terms of the number of lymph node retrieval; the improved OS did not reach statistical significance. Moreover, they also noticed that treatment with adjuvant chemotherapy was associated with improved OS (HR 0.491; 95% CI 0.248–0.708; P=0.001).[13]

In a propensity score matched one to one comparative analysis of Laparoscopic RAMPS with artery first approach (LaRAMPS) versus open RAMPS with artery first approach (OaRAMPS) it was seen that LaRAMPS was associated with less intraoperative blood loss (30vs.220g,p <0.001) and hospital stay (12vs.16days,p=0.049) and there was no serious intraoperative events requiring conversion to the open procedure. However, the total number of lymph nodes dissected and those harvested from around the SMA and R0 resection and postoperative adverse events, rates of CR-POPF were similar in both study groups. Information regarding long term survival was not available in this study.[7]

Sohal and colleagues looked into the National Cancer Database, USA to evaluate the relationship of tumor site with benefit from adjunctive (adjuvant, neoadjuvant, perioperative) therapy for patients with Stage I and Stage II pancreatic cancers treated between 2003-2013. A total of 27,930 patients met inclusion criteria; primary site was coded as head (74.4%), body (9.3%), or tail (16.3%). Pathologic stage was predominantly stage II (77%); 81% had negative margins. Perioperative chemotherapy was used in 4%, neoadjuvant in 8%, adjuvant in 48%. Median OS for the cohort was 24 months; for head, body and tail tumors it was 21.6 months, 34.5 months, and 42.5 months, respectively. On univariate analyses, adjuvant treatment was associated with improved OS for all the tumour locations; but on multivariate analysis the hazard ratio (HR) for adjuvant chemotherapy for head tumours was 0.66, CI: 0.63-0.70, p <0.0001, for body tumours was 0.89 CI: 0.76-1.04, p=0.15 and for tumours of pancreatic tail was 0.99, CI: 0.88 - 1.13, p= 0.92.[27]

Another analysis studied the role of radiotherapy in postoperative pancreatic cancers using the Epidemiology, and End Results (SEER) database from 2004 to 2015. Among 7097 patients, 2276 received adjuvant external beam radiotherapy and 4821 did not. Multivariate analysis revealed that race, age, median income, sex, year of diagnosis, American Joint Committee on Cancer (AJCC) T stage, N stage, regional lymph node involvement, chemotherapy, and radiotherapy were independent predictors for overall survival of all the patients (p < 0.05). After propensity score matching, a total of 4304 patients were included, 2152 in each arm. There was no OS and cancer specific survival benefit of

radiotherapy compared with no-radiotherapy (all $p > 0.05$). Radiotherapy reduced the all-cause mortality rate and cancer-specific mortality rate among patients with the N1 stage and T4 stage ($p < 0.05$). This analysis did not demonstrate any survival benefit for adjuvant radiotherapy for pancreatic body-tail cancer patients who have undergone upfront radical surgery emphasizing the need for personalized treatment decision on adjuvant radiotherapy in this group of patients.[16]

Our study involved moderately differentiated adenocarcinoma presented at relatively advanced stage and treatment with RAMPS and adjuvant chemoradiotherapy was associated with an acceptable survival rates. The only patient turned out to be benign solid pseudopapillary epithelial tumour of pancreas could have been treated with conventional distal pancreatico-splenectomy as per radiological diagnosis performed preoperatively, but because of its huge size and known malignant potential of this kind of tumour, although trivial,[28-29] a radical antegrade approach was followed.

Limitation of this study: Inclusion of very small number of patients and absence of a comparative arm.

CONCLUSION

RAMPS is a safe technique for resection of pancreatic body-tail tumours without added morbidities and might offer survival benefit over conventional distal pancreatico-splenectomy. RAMPS is also associated with improved tangential resection margin achieving high rates of R0 resections; but, it seems that OS depends largely on tumour biology.

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Authors' contributions

Rinki Das – Conceptualization, data collection, design and preparation of manuscript, manuscript editing

Ritankar Sengupta - Conceptualization, critical review and final approval.

Saurabh Das - Data collection, data analysis, manuscript editing

Tanup Das- Data collection, data analysis

Doyel Halder - Data collection, critical review

Parul Jain – Data collection, critical review

Asim Kumar Manna - Critical review and final approval.

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