COMPARISON OF ROBOTIC VERSUS OPEN AND LAPAROSCOPIC DISTAL PANCREATECTOMY IN PANCREATIC NEUROENDOCRINE TUMOR

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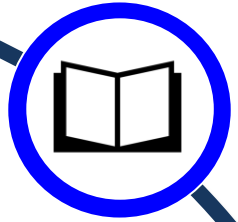
OUTLINE



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01 INTRODUCTION

PANCREATIC NEUROENDOCRINE TUMOR (PNET)

DEMOGRAPHICS

PNET occurs in 1-2% of pancreatic tumors, with the incidence of 2-3/100.000, mostly in the age group of 40-60 years old

SUBTYPES

PNET can be broadly divided into 2 subcategories, which are functioning (hormone producing) or non-functioning tumors depending on which gut peptides they secrete

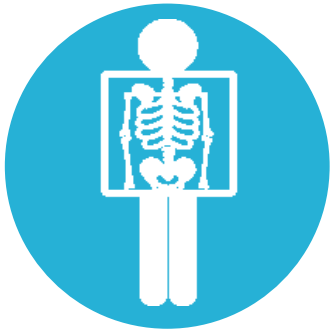
PATHOGENESIS

Most of pNETs occur sporadically, however approximately 10% may be associated with multiple neoplasia type 1 (MEN 1)

PANCREATIC NEUROENDOCRINE TUMOR (PNET)

CLINICAL PRESENTATION

Symptoms in non-functioning tumor can be caused by the mechanical problem from the tumor growth, while in functioning tumor, the symptoms are related to the hormone overproduction



DIAGNOSIS

Diagnosis of pNETs can be established through endocrine testing (gut hormone profile), imaging (CT, MRI, US, PET, EUS, SRS), and histological evidence

TREATMENT

Treatment for pNETs vary from surgery, medical therapy (based on tumor properties), systemic chemotherapy, or even surveillance

PANCREATIC NEUROENDOCRINE TUMOR (PNET)

Tumour	Frequency (%)	Location (%)	Malignancy (%)	Syndrome
Insulinoma	70-75	Pancreas (>99)	<10	Hypoglycaemia, Weight gain
Gastrinoma	20-25	Duodenum (70) Pancreas (25)	>50	Pain, diarrhoea, Ulceration
Vipoma	3-5	Pancreas (90)	>50	WDHA, Acidosis, Flushing
Glucagonoma	1-2	Pancreas (100)	>70	NME, Diabetes, Cachexia, Thrombosis
Somatostatinoma	<1	Pancreas (55) Duodenum/jejunum (45)	>50	Steatorrhoea, Diabetes, Gallstones, Weight loss
PPoma	<1	Pancreas (100)	>60	Pain, Weight loss, Diarrhoea
Bombesinoma	<1	Pancreas (100)	?	-
Non-functioning	90%	Panc + GI tract	>80	Mechanical problems, Tumour bulk

Table 1. Clinical presentation of pNETs based on the subtypes

PANCREATIC NEUROENDOCRINE TUMOR (PNET)

Biological behavior	WHO classification (2000)	WHO classification (2010)	Metastases	Invasion	Tumor size, cm	Angioinvasion	Ki67, %
Benign	Well-differentiated endocrine tumor	NET G1 or NET G2	–	–	≤2	–	usually around 2
Benign or low-grade malignant	Well-differentiated endocrine tumor	NET G1 or NET G2	–	–	>2	±	usually around 2
Low-grade malignant	Well-differentiated endocrine carcinoma	NET G1 or G2	+	+	any	+	usually >2
High-grade malignant	Poorly-differentiated endocrine carcinoma	NEC or G3	+	+	any	+	>20

NET = Neuroendocrine tumor; NEC = neuroendocrine carcinoma.

Table 2. WHO Classification for pNETs

DISTAL PANCREATECTOMY

DEFINITION

Removing the part of the pancreas extending to the left of the midline (not involving duodenum and distal bile duct)

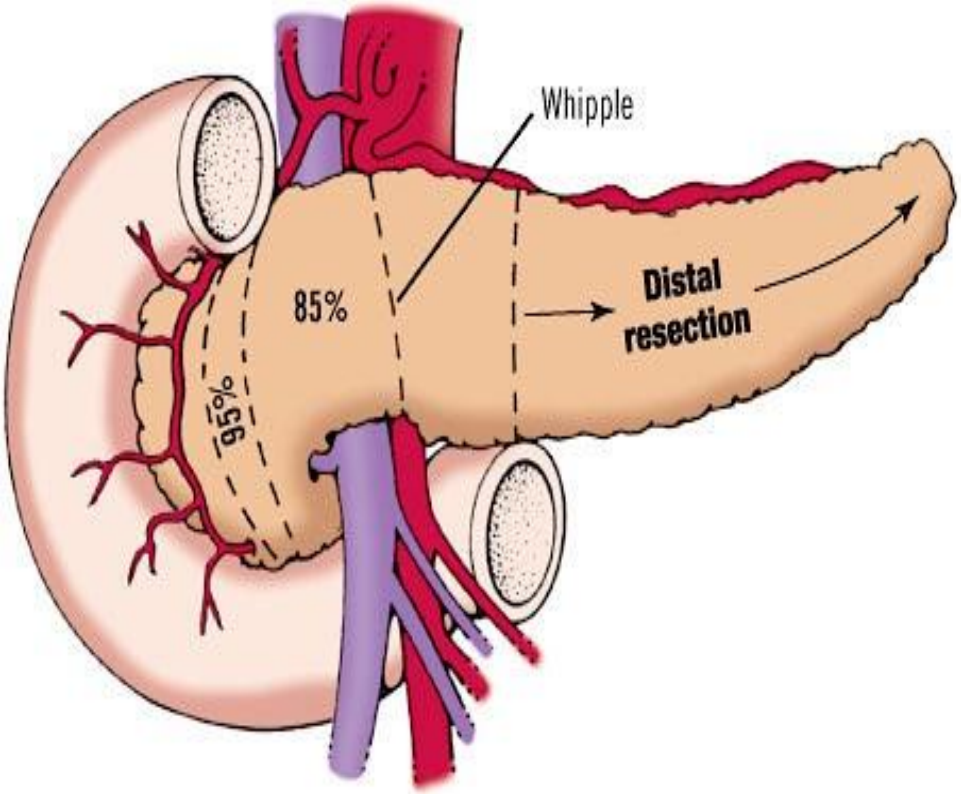


Figure 1. Distal pancreatectomy illustration

COMPLICATION

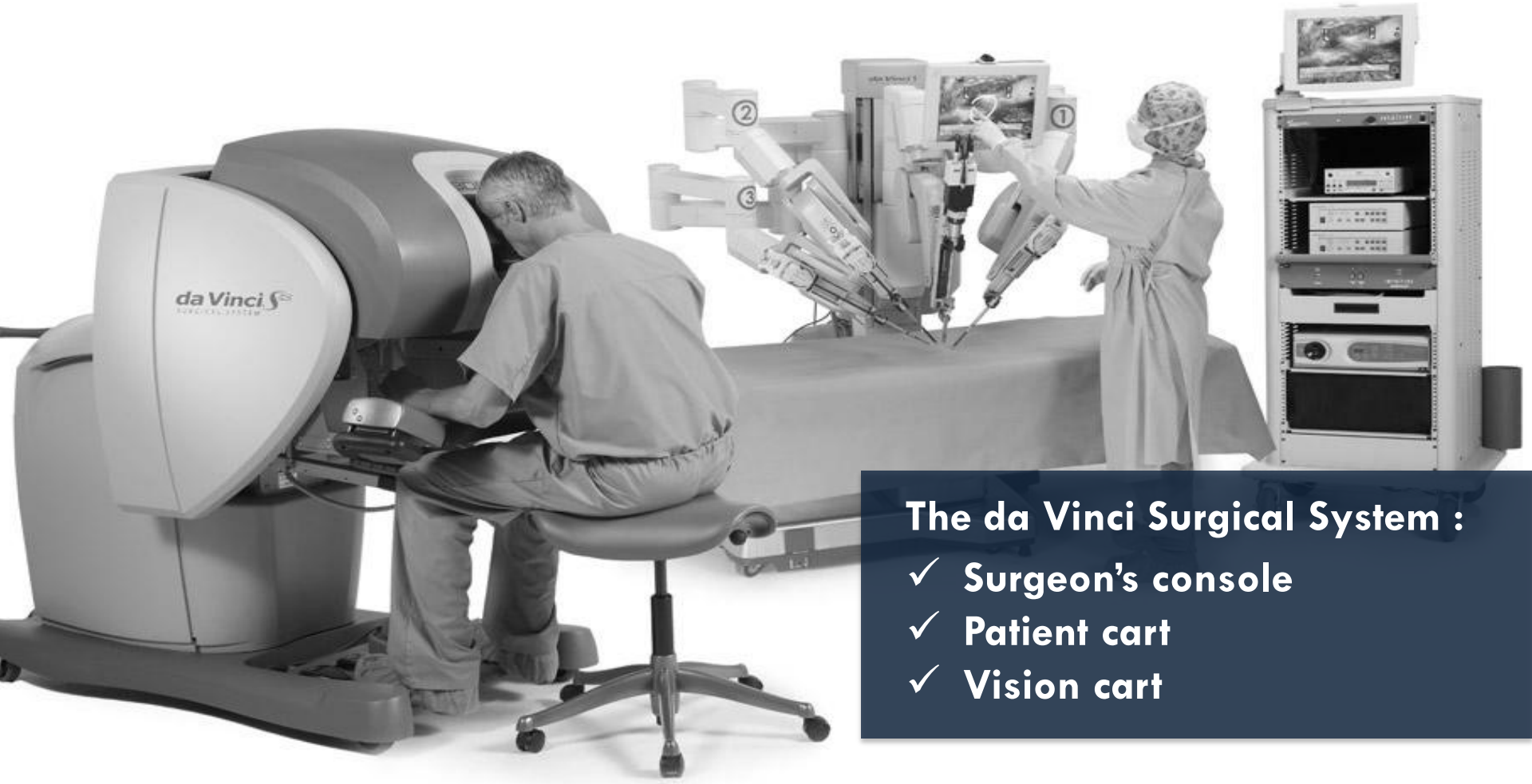
Post-operative pancreatic fistula (POPF) remains the most common complication following distal pancreatectomy

ROBOTIC SURGERY

Robotic surgery was claimed to be able to overcome the limitations of laparoscopic surgery

Robotic system enhanced surgeon's dexterity in many ways

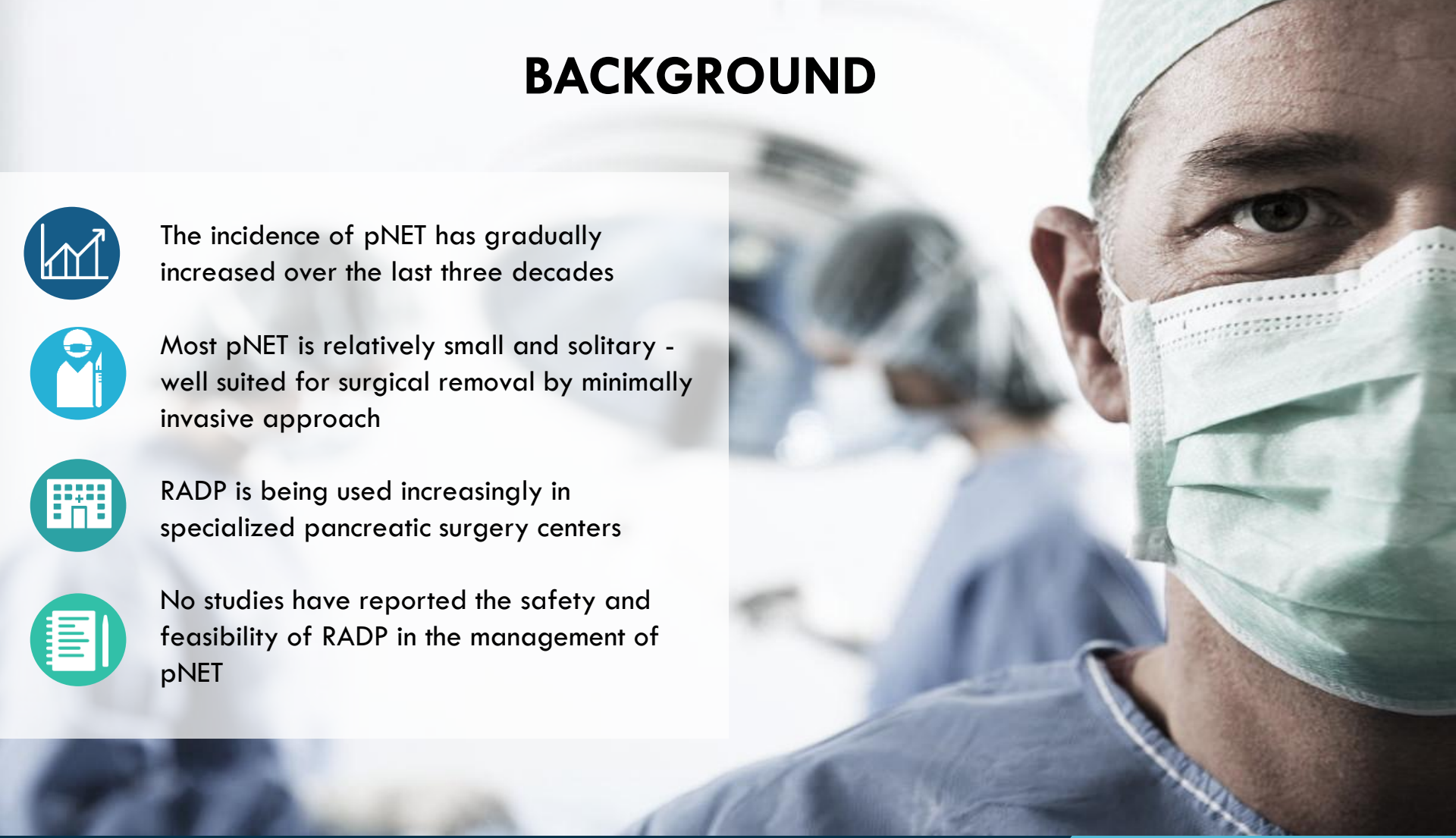
- 3 dimensional camera
- 7 degree freedom instrument
- Tremor and scale movement filter
- Endo-wrist technology
- Better ergonomics



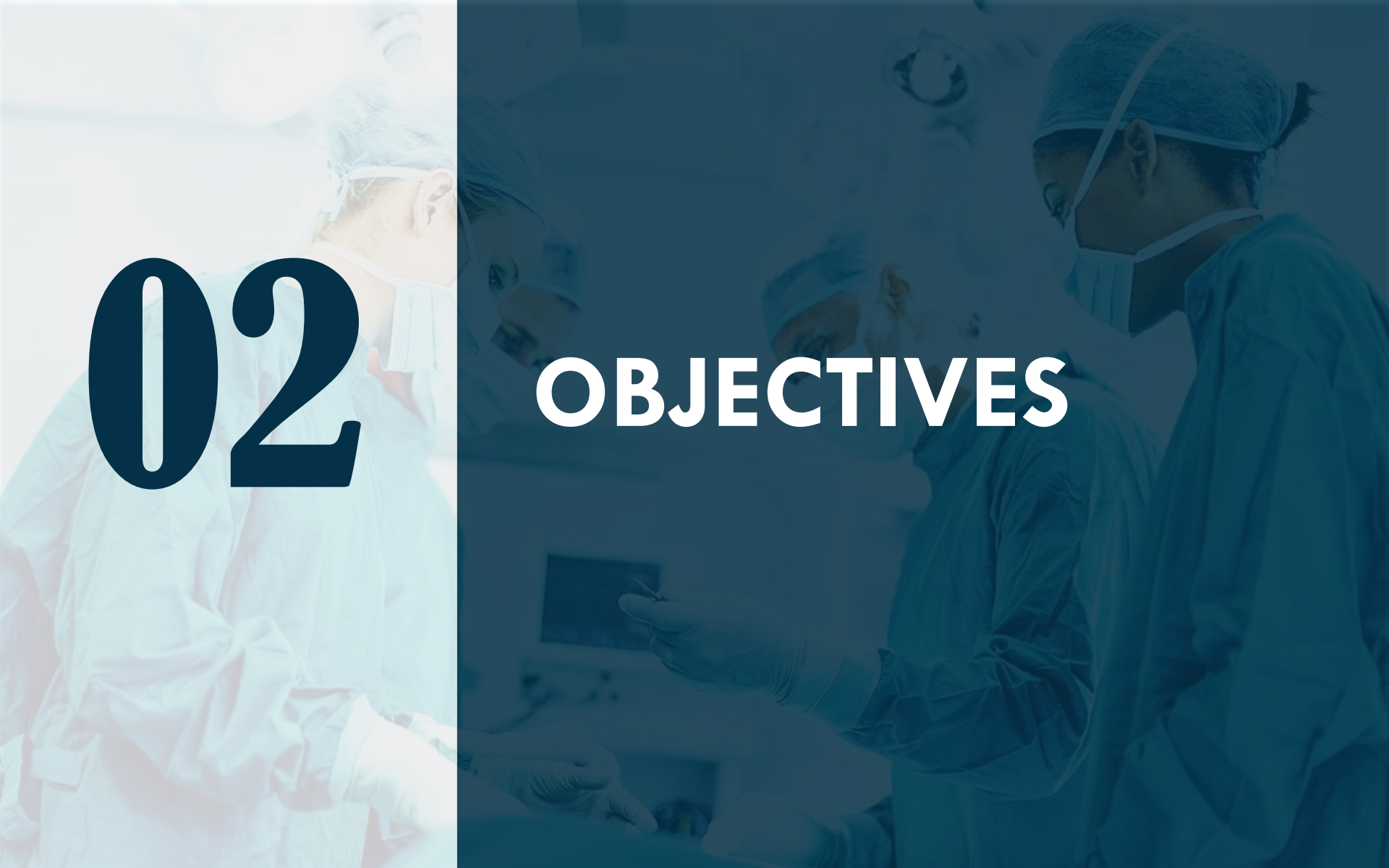
The da Vinci Surgical System :

- ✓ Surgeon's console
- ✓ Patient cart
- ✓ Vision cart

BACKGROUND



- The incidence of pNET has gradually increased over the last three decades
- Most pNET is relatively small and solitary - well suited for surgical removal by minimally invasive approach
- RADP is being used increasingly in specialized pancreatic surgery centers
- No studies have reported the safety and feasibility of RADP in the management of pNET



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OBJECTIVES

To conduct the first study which compares the outcomes of RADP, LDP, and ODP in PNET

To assess the safety and feasibility of robotic distal pancreatectomy in PNET

To verify the theoretical advantages of RADP over LDP and ODP in the clinical practices

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METHODS

DESIGN & STUDY POPULATION

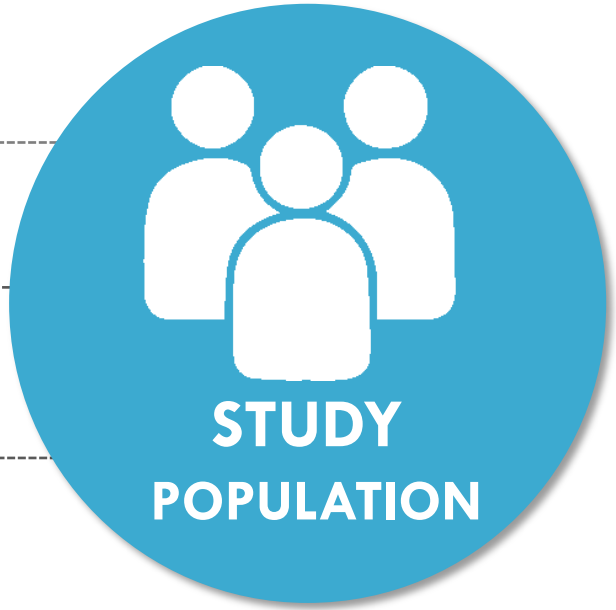
Decision on types of procedure was made in the MDT meeting

Follow-up was done through clinical examination, blood test, and imaging as needed

Patients undergoing ODP, LDP, RADP performed at HPB Surgery, Freeman Hospital (September 2007 - March 2017)

Inclusion criteria : patients undergoing distal pancreatectomy with or without splenectomy with the indication of pNET

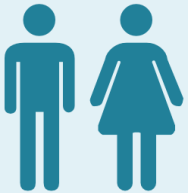
Exclusion criteria : patients who had another major procedure alongside the operation



DATA COLLECTION

Patients' medical records (electronic databases and patients' notes)

PATIENTS' DEMOGRAPHIC



- Age
- Gender

PATIENTS' CLINICAL DATA

- BMI
- ASA score
- Size of lesion
- Grade of lesion
- Ki67%

INTRA-OPERATIVE DATA

- Operative time
- Preparation time (for robotics)
- Estimated blood loss
- Spleen preservation rate
- Conversion rate
- Oncological outcome

POST-OPERATIVE DATA

- Total hospital stay
- Length of ITU stay
- 30-days morbidity
- Pancreatic fistula
- Post-operative DM
- 30-days reoperation
- 30-days readmission
- Recurrence
- Analgesia at discharge

DEFINITIONS

- **Ki67 =** Proliferation index for NET
- **CONVERSION =** Change of operative procedure from laparoscopic or robotic to open (laparotomy)
- **OPERATIVE TIME =** Time needed for the operation starting from the first incision until the skin closure
- **PREPARATION TIME =** Set-up time of the robot in the robotic group
- **R0 RESECTION RATE =** Complete excision of the tumor with the minimum clearance margin of 1 mm
- **MORBIDITY (30 DAYS) =** Clavien-Dindo Classification of surgical complication
- **PANCREATIC FISTULA =** ISGPF criteria
- **POST-OPERATIVE PAIN =** Morphine equivalent doses from discharged analgesia x daily frequency

Types of analgesia	Medications	Morphine equivalent dose
Non-opioid	Paracetamol (1000 mg)	-
	Nefopam (60 mg)	-
Weak opioid	Tramadol (50 mg)	5 mg
	Codeine phosphate (30 mg)	4.5 mg
	Dihydrocodeine (10 mg)	1 mg
Strong opioid	Morphine - Zomorph (10 mg)	10 mg

Table 3. Morphine equivalent doses

STATISTICAL ANALYSIS

P Value of less than 0.05 is considered statistically significant

All patients were analyzed on an intention-to-treat basis

CATEGORICAL DATA

- Reported in the form of frequency (percentage)
- Assessed using Chi - square (X^2) test

- Reported in the form of mean ± SD or median (range)
- Data normality was assessed by using Shapiro-Wilk test
- Assessed using ANOVA or Kruskal-Wallis test

CONTINUOUS DATA

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RESULT & DISCUSSION

PATIENTS' BASELINE CHARACTERISTICS

	Open DP n = 9	Laparoscopic DP n = 14	Robotic DP n = 10	*P* value
Age (years)	41 (17-73)	68.5 (32-76)	61.5 (34-72)	**0.03**
Sex				**0.031**
Female	6 (66.67 %)	4 (28.57 %)	8 (80%)	
Male	3 (33.33 %)	10 (71.43 %)	2 (20%)	
ASA score				**0.019**
1	2 (22.22%)	-	-	
2	5 (55.56%)	9 (64.29%)	2 (20%)	
3	2 (22.22%)	5 (35.72%)	8 (80%)	
Size of lesion (mm)	32.11±15.34	18.07±4.78	17.47±8.83	**0.003**

Table 4. Characteristic of patients undergoing distal pancreatic resection with pNET

Patients' gender, grade of lesion, and Ki67% of the lesion were similar between the three groups

INTRA-OPERATIVE VARIABLES

	Open DP n = 9	Laparoscopic DP n = 14	Robotic DP n = 10	*P* value
Conversion	-	2 (14.29%)	-	0.236
Operative time (min)	179.56±91.19	268.14±93.15	305.5±118.09	**0.031**
Preparation time (min)	-	-	46.8±15.46	
Estimated blood loss (ml)	930±402.82	467.5±283.89	410±127.28	0.074
Spleen preservation	7 (77.79%)	-	4 (40%)	**0.001**
Oncological outcome				
R0 resection	6 (66.67%)	13 (92.86%)	9 (90%)	0.2
Resection margin (mm)	1 (0-41)	2.75 (0-10)	2.8 (0-6)	0.079
Lymph node harvested	8 (0-27)	12 (4-56)	8 (0-14)	0.176

Table 5. Intra-operative outcomes of patients undergoing distal pancreatic resection with pNET

POST-OPERATIVE VARIABLES

	Open DP n = 9	Laparoscopic DP n = 14	Robotic DP n = 10	*P* value
ITU stay (days)	1 (1-20)	1	1 (1-4)	0.073
Length of stay (days)	11 (6-49)	8 (4-34)	9 (5-16)	0.292
30 days morbidity	4 (44.44%)	6 (43.86%)	7 (70%)	0.374
Major complication (Clavien-Dindo Grade 3,4)	2 (50%)	4 (66.67%)	-	**0.034**
Minor complication (Clavien-Dindo Grade 1,2)	2 (50%)	2 (33.33%)	7 (100%)	
Pancreatic fistula	4 (44.44%)	5 (55.56%)	6 (60%)	0.227
ISGPF grade				0.078
Low Grade (A,B)	2 (50%)	2 (40%)	6 (100%)	
High Grade (C)	2 (50%)	3 (60%)	-	
Post-operative DM	-	6 (42.86%)	1 (10%)	**0.029**

Table 6of patients undergoing distal pancreatic resection with pNET

POST-OPERATIVE VARIABLES

	Open DP n = 9	Laparoscopic DP n = 14	Robotic DP n = 10	*P* value
Reoperation (30 days)	2 (22.22%)	1 (7.14%)	-	0.23
Readmission (30 days)	3 (33.33%)	7 (50%)	1 (10%)	0.122
Recurrence	1 (11.11%)	1 (7.14%)	-	0.584
Post-operative drain removal (days)	9 (5-37)	6 (3-42)	14 (6-44)	**0.014**
Analgesia at discharge	7 (77.78%)	11 (78.57%)	10 (100%)	0.277
Non-opioid	7 (100%)	10 (100%)	10 (100%)	1
Weak opioid	6 (85.71%)	6 (64.55%)	2 (20%)	**0.026**
Strong opioid	-	-	1 (10%)	0.393
Morphine equivalent (mg)	31.67±9.83	26.67±10.33	22.67±6.43	0.287

Table 6b. Post-operative outcomes of patients undergoing distal pancreatic resection with pNET

Patients' follow-up varied from 18(1-69) months

BENEFITS OF ROBOTIC SURGERY

Less estimated blood loss

Better hemostasis, and control of splenic artery, portal and mesenteric blood vessels, and the other small vascular network located near the pancreas

Higher spleen preservation

Palep et al : 3D visualization & motion tremor filter results in better accuracy in complex surgical task

Higher R0 resection rate

Surgeons claimed that this was resulted from the better ergonomics in RADP

Less major complication

Contributed to the technological advantages in the robotic system

Less post-op DM

Higher accuracy in robotic system, as well as the extent and location of the resection may affect the insulin secretion that play role in the occurrence of pancreatic diabetes

Less weak opioid prescribed

Less post-operative pain experienced by the patients

DISADVANTAGES OF ROBOTIC SURGERY

This may be related to the surgical learning curve, setup time, and the time required in adapting to a new technology and technique

With more experience, this can be quickly reduced, Napoli et al - 10 cases, Shakir et al - 40 cases

Longer operative time

Possible higher cost

Not calculated in our study

Kang et al – RADP vs LDP : 8304$ vs 3861$

Butturini et al – RADP vs LDP : 10588$ vs 12986$ due to shorter hospital stay

05

CONCLUSION

Robotic distal pancreatectomy has unique advantages over laparoscopic and open approach in the management of pNET and should be considered where appropriate surgical expertise exists

Its safety and feasibility are comparable with the other two techniques as shown by the lower trend in blood loss, similar R0 resection rate, lower post-operative diabetes mellitus, lower high-grade complication, and lower high-grade fistula

The major disadvantages are the increased cost and operative time

THANK YOU

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