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Faculty of Medicine, Cairo University Postgraduate Research Protocol Template

1. Study

a- Proposed Study Title:

Total laparoscopic versus open pancreaticoduodenectomy: a prospective comparative randomized clinical study

دراسة استباقية لمقارنة اوجه الفروق بين استئصال اورام البنكرياس والاثنى عشر بالمنظار او الفتح الجراحي

b- Degree: MD

c- Date of Registration of MD: Jan 2022

3. Scientific committee approval :

Date of approval: 1/9/2022 , code MD-196-2022

4. Background and Rationale:

Total laparoscopic pancreaticoduodenectomy (TLPD) remains one of the most advanced laparoscopic procedures. Owing to the evolution in laparoscopic technology and instrumentation within the past decade, laparoscopic pancreaticoduodenectomy is beginning to gain wider acceptance.(1)

Gagner and Pomp were the first to describe the laparoscopic Whipple procedure in 1994.[3] The long operative times and technical difficulties coupled with the need to develop advanced laparoscopic skills[1,2] were valid reasons that supported the initial reluctance to pursue these sophisticated minimally invasive operations. Recently, laparoscopic pancreaticoduodenectomy has started to gain wider acceptance as surgeons become more comfortable with laparoscopic technology. As a result, TLPDs have been reported with an increased frequency from institutions internationally.(2-15)

In recent years, total laparoscopic pancreaticoduodenectomy (TLPD) has been introduced as a feasible alternative to open pancreaticoduodenectomy (OPD) when performed by experienced surgeons in laparoscopic and pancreatic surgery. Its application has been gradually increased, but its safety, reproducibility, and oncological outcomes are still debated due to its technical complexity and prolonged operating time. There are different experiences present in the literature regarding indications, surgical techniques, postoperative outcomes, benefits and limitations of this approach, oncological results, learning curve, and costs. There is no standardized surgical technique for TLPD. Different techniques exist for both the demolitive stage and the reconstructive stage. We summarized the different aspects of the surgical technique based on the various experiences reported by different authors. Compared to OPD, TLPD provides the advantages of laparoscopy, i.e., reduced blood loss, decreased postoperative pain, and shorter length of hospital stay, without increasing the rate of postoperative complications or compromising oncological outcomes. With increased experience, more challenging cases may also be approached with this technique, including those requiring major vascular resections or multi-visceral resections.(16)

Pancreaticoduodenectomy (PD) has seen improved perioperative outcomes and complication rates over the last few decades (17-20). Nevertheless, it continues to be a morbid operation with complications ranging from 24-59% (21-23). Laparoscopic surgery reduces surgical morbidity in various operations, however laparoscopic pancreaticoduodenectomy (LPD) is a relatively new procedure which lacks a clear consensus regarding its benefits (24-28). Although the first published case was described in 1994, it has been slow to gain popularity (29). This is likely in part due to the challenging technical aspect of the procedure including the retroperitoneal location of the pancreas, close vicinity to the superior mesenteric artery and vein, portal vein and hepatic arteries and the technical difficulty of three anastamosis. In recent years, however, we have seen an increasing

number of studies examining LPD. Initial research evaluated feasibility and outcomes, assessing whether LPD could be done with adequate safety (30-37). The question then moved to compare to the open approach questioning if it will it appreciate the same benefits of other laparoscopic surgeries. Partially enabled by higher volumes at specialized centers, studies began comparing LPD with (OPD). Although there are a handful of pancreaticoduodenectomy review articles evaluating LPD in the literature, many include papers with limited sample sizes and case reports. Our goal in this study is to compare and contrast the outcomes of both approaches aiming to reduce post operative morbidity and oncological outcomes.

5. Objectives:

The study aims to determine the advantages and disadvantages of performing total laparoscopic pancreaticoduodenectomy over the open approach and to compare the outcomes aiming to reduce the magnitude of operative morbidity.

6. Study Design:

Prospective comparative randomized clinical study

- **Study Methods**
- **Population of study:**

Patients presenting to Kasr Al-Ainy hospital requiring pancreaticoduodenectomy

- **Study location:**

Kasr AlAiny Hospitals – Cairo University

- **Inclusion criteria:**
  - Patients presenting with pancreatic head tumours, cholagiocarcinoma, duodenal tumours (1st, 2nd and 3rd part) and ampullary tumours who are fit for either open or laparoscopic pancreaticoduodenectomy
- **Exclusion criteria:**
  - Patients who are deemed inoperable due to the presence of metastases

- Patients with irresectable tumours

- **Methodology in details:**

  - Patients will present to the outpatient clinic of Kasr Alainy hospitals with pancreatic head tumours, cholagiocarcinoma, duodenal tumours (1st, 2nd and 3rd part) and ampullary tumours who are fit for either open or laparoscopic pancreaticoduodenectomy.
  - Full assessment will be done by clinical examination, radiological assessment in the form of EUS, CT scan and metastatic work-up, laboratory investigations in the form of tumour markers and tissue biopsy histopathological examination.
  - Patients will be classified into frank resectable, bordeline resectable (defined as pancreatic head masses larger than 4 cm in size, equivocal findings of ascites and metastases on CT scan and signs of advanced disease as in marked weight loss and markedly elevated CA19-9 > 1000) and frank irresectable.
  - A decision will be made by the multidisciplinary team and patients will be selected to undergo total laparoscopic pancreaticoduodenectomy or open pancreaticoduodenectomy through a randomized manner
  - Patients with tumours classified as borderline resectable tumours will be subjected to diagnostic laparoscpy prior to open suregry
  - A diagnostic survey and intraoperative ultrasonography were performed to assess for resectability and other pathological conditions such as the presence of ascites, liver metastases and peritoneal deposits and a decision to proceed or abort will be made accordingly.
  - Patients classified as bordeline resectable will undergo an intraoperartive ultrasound assesment of the vessel involvement, LNs and tumour size if irresectability is suspected.
  - Open approach will entail a roof top incision
  - Laparoscopic approach will entail trocar placement at the following sites:
    - 10 mm visual port at the level of the umbilicus
    - 12 mm port in the right mid-clavicular line 2 cm below the umbilicus
    - 5 mm port in the left mid-clavicular line 2 cm below the umbilicus
    - 5 mml port in the right mid-calvicular line 2 cm above the umbilicus
    - 5 mml port in the left mid-clavicular line 2 cm above the umbilicus
    - An optional 5mm port in the epigastric region if required
  - Total internal stents will be placed inside the pancreatic and biliary anastomoses. The size of the stents will be determined according to caliber of pancreatic duct and common bile duct.
  - Operative time will be calculated in minutes starting from skin incision to skin closure

- Blood loss will be assessed in coordination with the anaethesia team by counting the number of soaked towels and gauze and calculating the amount of blood suctioned through out the procedure.
- Daily chest assessment to exclude or suspect lung atelectasis, pleural effusion or pneumonia will be done. Further chest imaging and will be done if required.
- Daily serial abdominal examination to exclude or suspect pancreatic or biliary leakage will be done. Further laboratory assessment will be done if required (inflammatory markes: TLC, CRP, serum and drain amylase, serum and drain blilirubin), imaging in the form of an abdomen and pelvis CT study may be done if required.
- Daily wound assesment will be done starting 48 hours following surgery
- Pain assessment will done by means of a visual analogue scale (VAS)
- Early patient satisfaction in terms of post operative pain, early ambulation, ability to resume daily activities and complicatons by means of a questionnaire
- ICU stay and total hospital stay will be calculated
- Pathological assessment will be noted in terms of number of Lns harvested and the resection margins (R0 or R1)
- Incison / portsite examination to exclude incisional or portsite hernia.

- **Does the research involve?**

■ Human participants

☐ Biological samples/Tissues

☐ Identifiable private data/Information

- **Type of consent of study participants:**

■ Written consent

☐ Oral consent

☐

No consent needed (Please justify)

- **Potential risks:**

No attributed risks can be related to the study

- **Confidentiality of data:**

All study related information will be stored securely at the study site.
All participant information will be stored in locked file cabinets in areas with limited access.
Participants' study information will not be released outside the study without the written permission of the participant.
Research ethics committee "REC" & Health authorities have the right to review's patient's data

9- Study outcomes:

- **Primary outcome:**

- Operative time
- Assessment of early post-operative complications including: pain, respiratory complications (collapse, pleural effusion or pneumonia)
- Incidence of pancreatic and biliary leakage

- **Secondary outcome:**

- ICU stay and total hospital stay
- Patient satisfaction in terms of pain, ambulation, ability to resume daily routine activities
- Blood loss and need for blood transfusion accordingly

- Wound complications including: infection (early) and incisional hernia/port site hernia (late)
- Pathological assessment in terms of LN harvesting and resection margins (R0 resection or R1)

10- Sample size

The sample size was assessed using the G ∗ power 3.1.9.4 software (Universities Kiel, Germany). The calculation was based on the study of Ammori et al. [11], which reported a mean hospital stay length of 4.7 ± 1.125 days in the OPD group compared to a respective mean of 8.9 ± 5.425 days in the LPD group. After setting the study power at 80% and α at 0.05, a minimum of 12 patients in each group were required.

11- Statistical analysis

12- Source of funding:

- No Funding

13- Time plan:

- When to start? After REC approval

- When expected to finish?

- When to publish?

14- References:

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