



Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: <http://www.clinicalnutritionespen.com>

Original article

## Sarcopenia is associated with a greater incidence of delayed gastric emptying following pancreaticoduodenectomy

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### ARTICLE INFO

#### Article history:

Received 17 May 2018

Accepted 26 May 2018

#### Keywords:

Delayed gastric emptying  
Pancreaticoduodenectomy  
Complication

### SUMMARY

**Background and aims:** Sarcopenia is the degenerative loss of skeletal muscle and has been associated with a variety of post-operative complications. We propose sarcopenia is associated with delayed gastric emptying (DGE) following elective pancreaticoduodenectomy (PD).

**Methods:** A retrospective analysis of a computerised database maintained in real time of all patients undergoing PD within our hepatobiliary unit was performed. The cross-sectional area of the psoas muscle at the upper border of L3 was calculated and corrected for patient height. The lowest quartile of gender specific groups was considered to be sarcopenic.

**Results:** 61 patients were included, 32 male and 29 female of whom 8 from each group were sarcopenic (26.2%). Although the sarcopenic and non-sarcopenia groups were found to be comparable, significantly more sarcopenic patients were older (75 vs 64 years,  $p = 0.003$ ), had a lower body mass index (21.9 vs 25.0 kg/m<sup>2</sup>,  $p = 0.003$ ) and suffered from DGE (7/16 vs 8/45,  $p = 0.045$ ). On multivariate analysis, these variables maintained their significance with DGE having an OR of 6.042 ( $p = 0.036$ ).

**Conclusion:** Sarcopenia is significantly associated with DGE, older age and lower BMI in this specific cohort of patients. Further research into the reversibility of this phenomenon is warranted.

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### 1. Introduction

Pancreaticoduodenectomy (PD) is the mainstay of surgical treatment for localised pancreatic and periampullary malignancy [1]. However, despite the advancements in surgical technique and perioperative care, post-operative morbidity still affects up to 65% of patients [2]. Such complications can prevent the timely administration of adjuvant therapies [3,4]. Alongside pancreatic fistula, delayed gastric emptying (DGE) is one of the leading causes of morbidity after PD. With incidence ranging between 8 and 45% [5] it serves as one of the main complications delaying further treatment.

In order to align patient hopes with expectations and usher patients quickly towards adjuvant therapy, predicting and avoiding these complications is paramount. Whereas considerable advancements have been made in identifying factors associated with

pancreatic fistula following PD [6], efforts to predict patients at risk of DGE have been inconsistent [7]. It has been postulated that the cause of DGE is likely multifactorial and has been associated with intra-abdominal and respiratory complications [8,9], altered neuro-hormonal pathways [10] and approach to anatomical reconstruction [11]. Yet none of these have been shown to consistently predict the incidence of DGE.

A novel variable associated with post-operative complications in a variety of surgical fields is the presence of sarcopenia. Defined as loss of skeletal muscle resulting in decreased strength and general physical performance with impaired resilience to stress [12], sarcopenia is found in almost 80% of cancer patients [13,14]. It is associated with decreased survival and increased recurrence rates in multiple types of malignancy [15] including carcinoma of pancreatic origin [16,17]. Sarcopenia has also been associated with increased complications after PD including pancreatic fistula [18]. However, the relationship between this phenomenon and DGE is less well understood.

Using single slice computed tomography (CT) to measure the cross sectional diameter of psoas muscle has been validated as

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means to calculate total body muscle mass [19]. A trend has thus emerged to use the cross-sectional diameter of psoas as a proxy for sarcopenia. This measurement is known as total psoas area (TPA) and despite its limitations [20] has been widely used as a proxy for total body muscle mass [21–23].

The aim of this study was to determine whether sarcopenia as measured by TPA was associated with a greater incidence of DGE in patients following elective PD for tumours at the head of the pancreas.

## 2. Materials and methods

This retrospective study was undertaken at the Shaare Tzedek Medical Centre in Jerusalem. This one thousand bed university affiliated hospital has two dedicated hepatobiliary surgeons (MBH, AD). Institutional ethics board approval was attained who waived the requirement for patient consent in light of the retrospective nature of the study.

All consecutive patients undergoing PD with curative intent in our department between December 2014 and February 2017 were enrolled in a digital database maintained in real time which was retrospectively analysed. This digital cohort included 83 patients. There were several inclusion criteria for the study. Firstly, a contrast enhanced abdominal CT must have been performed within 30 days of the index surgery that was accessible for review. This excluded 19 patients. Patients must also have survived the index admission as a subset analysis of the 2 patients who did not revealed all were admitted post-operatively to the intensive care unit (ICU) intubated after surgery and never resumed an oral diet before they died. This left a final cohort of 61 patients.

All patients that were included in the study were managed according to a standardised enhanced recovery protocol and underwent the same reconstructive technique. Pre-operative preparation included prophylactic intravenous antibiotics and subcutaneous low molecular weight heparin. No routine bowel preparation was used. For the reconstruction, a single limb Roux-en-Y retrocolic end-to-side two layered pancreatico-jejunostomy and single layered hepatico-jejunostomy was performed. The pylorus was not routinely preserved with antrectomy achieved using a linear stapler and reconstructed using an ante-colic hand-sewn gastro-jejunostomy. Two Jackson Pratt drains are routinely placed adjacent to the pancreatic and biliary anastomoses. Patients were monitored overnight in the surgical ICU before being transferred to the ward if stable. Nasogastric tubes were routinely removed at the end of surgery and early oral intake and ambulation encouraged. Nasogastric tubes were re-inserted if the patient was persistently nauseated or vomited and subsequently removed when the volume of effluent decreased. Parenteral and total parenteral nutrition was not routinely used.

In order to identify whether sarcopenia was associated with a greater incidence of DGE, demographic data and pre-, intra-, and post-operative clinicopathological variables were collated from the computerised database. Both DGE [8] and pancreatic [24] fistula were graded according to the International Study Group of Pancreatic Surgery Consensus definition. Pancreatic fistulas were considered clinically relevant if they were graded either B or C. All grades of DGE were included in the study. Serious post-operative complications graded as Clavien-Dindo III or more were included in the analysis if they occurred within 30 days of surgery. ICU admission was included as a variable if the patient required more than 24 h in the ICU before returning to the ward.

In order to quantify sarcopenia, images of pre-operatively performed contrast enhanced abdominal CT were retrieved using the Picture Archive and Communication System (PACS). In order to standardize reading they were all reviewed for the purpose of this study by a single radiology resident (L.W.) supervised by a

consultant radiologist (I.H.). Both radiologists were blinded as to which patients suffered from DGE. The images were analysed using SW Application for PACS (GE Healthcare, Little Chalfont, United Kingdom). Using a free-hand circumferential region of interest tool the borders of the psoas muscles were delineated in the axial plane at the superior border of L3. This allowed the total psoas muscle area, in mm<sup>2</sup>, to be calculated. An average measurement of the right and left muscles was used in the final analysis. This TPA was then normalised for height, a process previously reported for the measurement of body composition (cm<sup>2</sup>/m<sup>2</sup>) [19,25].

A patient was defined as being sarcopenic if the average measurement of the total psoas muscle area corrected for height fell into the lowest quartile of the quartile as a whole for that gender group, a cut-off used by others [25].

Statistical analysis was performed using SPSS version 24 for PC (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to describe the study cohort with results expressed as median or frequency with standard deviation (SD) or percentages in parentheses unless stated otherwise. Comparisons made between categorical variables were performed using Fisher's exact test in light of the small sample size with Mann–Whitney U test for non-categorical variables. A *p* value of <0.05 was considered statistically significant and are written in italics. For those variables found to be statistically significant on univariate analysis, a multivariate stepwise regression model was created using binary logistic regression analysis using an 'enter' procedure. The effects of independent variables are listed as odds ratios (OR) with 95% confidence intervals (CI).

## 3. Results

In total, 61 patients met the inclusion criteria, 32 of whom were male and 29 female. Basic clinical and pathological data is presented in Table 1. With a median age of 71.5 years (SD 8.5), ductal

**Table 1**  
Clinicopathological data for the cohort of patients included in the study.

Variable	N (%) / Median (SD)
Demographic and pre-operative characteristics	
Gender	
Male	32 (52.5)
Female	29 (47.5)
Age (years)	71 (8.5)
Pre-operative albumin (g/dL)	3.6 (0.7)
Non-insulin dependant diabetes mellitus	25 (40.9)
Charlson Score	1.7 (6.4)
Ca 19-9 >37U/mL	30 (49.2)
Body Mass Index (BMI) (Kg/m <sup>2</sup> )	24.1 (13.1)
Tumour characteristics	
Underlying pathology	
Ductal adenocarcinoma	34 (55.7)
Other	27 (44.3)
Differentiation	
Well	8 (13.1)
Moderate	32 (52.5)
Poor	10 (16.4)
Stage of tumour	
T1	7 (11.5)
T2	11 (18.0)
T3	33 (54.1)
T4	1 (1.6)
Lymph node disease	30 (49.2)
Neoadjuvant therapy	3 (4.9)
Surgical characteristics	
Vascular resection	12 (19.7)
Pylorus preserving procedures	2 (3.3)
Pancreatic gland texture	
Soft	34 (55.7)
Firm	27 (44.3)
Length of hospital stay (days)	12 (17.9)

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