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Research Article

Sarcopenia as a Predictor of Postoperative Complications and Pancreatic Fistula in Patients with Pancreatic Cancer

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Abstract

Objective: To determine the impact of sarcopenia on the occurrence of postoperative complications and pancreatic fistula after pancreatic resection in patients with pancreatic cancer.

Materials and Methods: Retrospective study of treatment of 143 patients with pancreatic cancer, who underwent pancreaticoduodenectomy in our Institute was performed in the period from 2016 till 2018. Preoperative computed tomography (CT) was done for all patients. Sarcopenia was quantified using the Total Psoas Index (TPI). The measurements were conducted at the level of the third lumbar vertebral body (L3).

Results: Sarcopenia was diagnosed in 66 (44.9%) patients using TPI, postoperative complications occurred in 40 (60.6%) patients, in patients without sarcopenia postoperative complications occurred in 27 (33.3%) patients ($\chi^2 = 10.9$, $p = 0.001$). Mortality was 4 (6.0%) and 2 (2.5%) respectively ($\chi^2 = 1.2$, $p = 0.3$). In patients with sarcopenia infectious complications occurred in 7 patients, pancreatic fistula Grade B or Grade C - in 22, haemorrhage - in 9 patients, delayed gastric emptying in 2. In patients without sarcopenia infectious complications occurred in 6 patients, pancreatic fistula Grade B or Grade C - in 8, haemorrhage - in 8, chyle leak - in 3 patients. We didn't find any significant difference in the number of infectious complications ($\chi^2 = 0.2$, $p = 0.6$), delayed gastric emptying ($\chi^2 = 0.2$, $p = 0.7$) and haemorrhage ($\chi^2 = 0.4$, $p = 0.5$), but the level of pancreatic fistula Grade B or Grade C was significantly higher ($\chi^2 = 4.2$, $p = 0.04$) in patients with sarcopenia.

Conclusion: TPI could be easily calculated preoperatively in patients with pancreatic cancer. Present results suggest that sarcopenia is a reliable indicator of the surgical outcome and significantly affects the level of postoperative complications and can be used to improve the selection of patients with pancreatic cancer prior to resection.

Keywords: *Daily pH-Metry; Hydrogen Ion Concentration H+*

Introduction

Pancreatic cancer is an aggressive malignancy and is currently the fourth most common cause of cancer-related mortality in the economically developed world and is set to become the second most common cause of cancer-related mortality within the next few years [1]. The number of patients with pancreatic cancer in Ukraine is increasing year by year, in particular patients with advanced cancer. Radical surgical resection in combination with systemic chemotherapy offers the only hope of cure or long-term survival in patients with pancreatic cancer with 5-year survival ranging from 10 to 20% [1-3].

Despite recent improvements in diagnosis, in operative technique and perioperative care mortality has decreased to less than 5% at high volume centers but morbidity still remains high at 40 - 60% [4-6].

Since the general condition of the patient in the postoperative period affects the timing of chemotherapy, it is very important to prevent postoperative complications.

Pancreatic fistulae, postoperative haemorrage, infectious complications after pancreatic resections can lead to fatal results. Thus, it is very important not only to recognize and cure complications, but also to improve methods aimed at preventing the development of post-operative complications before surgery [1-4].

According to the literature, in 1989, Irwin Rosenberg proposed the term "sarcopenia" (Greek 'sarx' or flesh + 'penia' or loss) to describe this age-related decrease of muscle mass. Sarcopenia has since been defined as the loss of skeletal muscle mass and strength that occurs with advancing age [6].

Sarcopenia is a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death [7,8].

According to the literature, the presence of sarcopenia has shown an impact on the occurrence of postoperative complications and the specific outcome of treatment of pancreatic cancer using multimodal antitumor therapy [7-10].

Therefore, the ability to predict the occurrence of postoperative complications in patients with pancreatic cancer can potentially improve patient selection and postoperative outcomes.

A number of techniques were worked out for determining sarcopenia with CT. Peter Peng and co-authors described sarcopenia measurements using the Total Psoas Index (TPI), which measured the area of the right and left large lumbar muscles at the level of the third lumbar vertebra and related it to the patient's height [7].

In our work, we calculated TPI for CT using the OsiriX 9 software.

Aim of the Study

To determine the impact of sarcopenia on the occurrence of postoperative complications and pancreatic fistula after pancreatic resection in patients with pancreatic cancer.

Materials and Methods

In total 143 patients with pancreatic cancer were analyzed on presents of sarcopenia in 2016 - 2018.

We performed 143 radical pancreatic resections in patients with pancreatic cancer: distal pancreatectomy in 17 (19.5%) patients, pancreaticoduodenectomy - in 67 (77.0%), total pancreatectomy - in 3 (3.5%) patients. The average age of patients was 55.9 ± 9.4 years (from 27 to 81).

Design of the study: It was a prospective study. We considered only patients with resectable pancreatic cancer and periampullary cancer: bile duct cancer, ampullary cancer, duodenal cancer, defined by absence of distant metastases, absence of local tumor extension to the celiac axis and hepatic artery as the lack of involvement of the superior mesenteric artery or vein and to the portal vein. None of these patients received neoadjuvant chemotherapy.

Inclusion criteria: Patients with resectable pancreatic cancer T1-3N0M0 or periampullary cancer T1-3N0M0.

Exclusion criteria: Patients with borderline resectable and locally advance pancreatic cancer, patients with cholangitis and endobiliary stenting or biliary drainage (retrograde or antegrade).

Standard examination was performed in all patients. We performed ultrasound, computed tomography in all cases and enhanced magnetic resonance imaging and endoscopic ultrasound if they were needed.

Preoperative computed tomography (CT) was performed for all patients with intravenous contrast no earlier than 6 weeks before surgery. Sarcopenia was quantified using the Total Psoas Index (TPI). The measurements were conducted at the level of the third lumbar vertebral body (L3).

The diagnosis was confirmed by postoperative morphological examination of the material. Pancreatic fistula was determined according International Study Group of Pancreatic Fistula. Delayed gastric emptying and hemorrhage were determined according International study group of pancreatic surgery. Infectious complications were confirmed if a positive result of microbiological examination was achieved. The sarcopenia was calculated using the Total Psoas Index (TPI) - the total lumbar muscle index.

The measurements were carried out in a semi-automated form with a manual outline of the limits of the large lumbar muscles at level 3 of the lumbar vertebra which automatically calculated the lumbar area. The measurement of the area of the large lumbar muscle was then correlated with the patient's height.

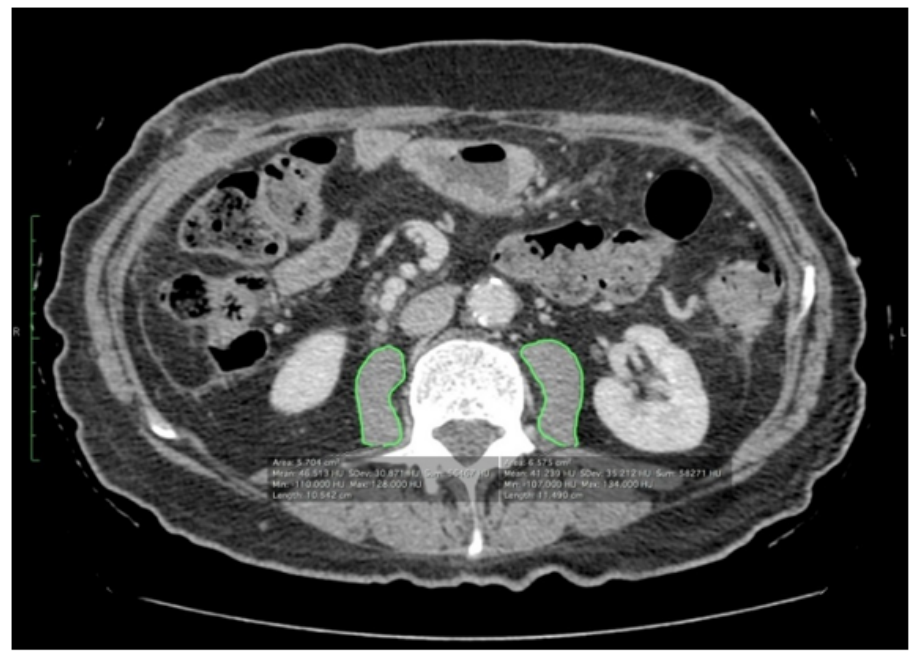

Figure 1: *CT scan with manual presentation of borders of large lumbar muscles at level 3 of lumbar vertebra.*

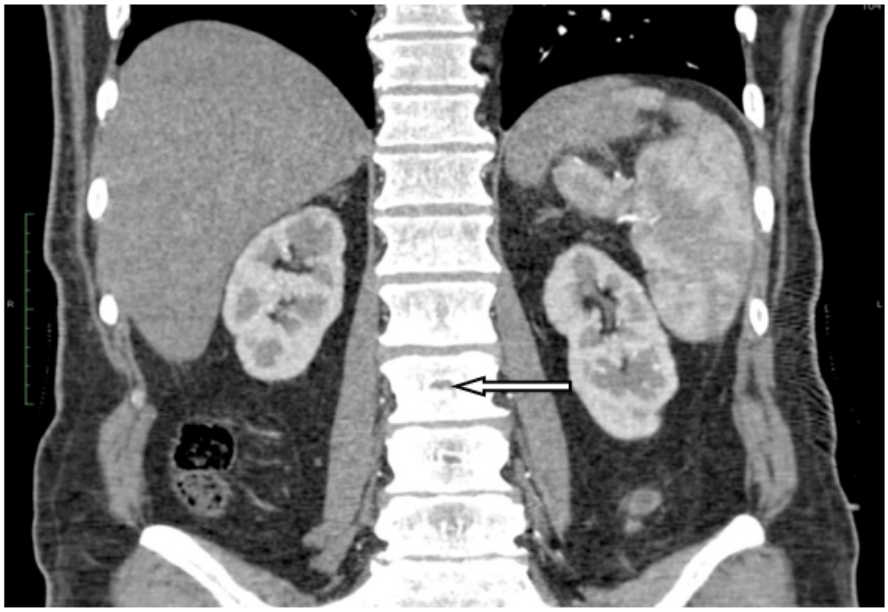

Figure 2: *CT with determination of level 3 of the lumbar vertebra.*

The TPI is calculated as follows: right musculus psoas area + left musculus psoas area divided by patient height in m^2.

For men sarcopenia was considered when the TPI was less than 5.2 cm^2/m^2, for women, TPI should be less than 4.0 cm^2/m^2.

Results

Sarcopenia was diagnosed in 66 (44.9%) patients. Postoperative complications occurred in 40 (60.6%) patients, in patients without sarcopenia postoperative complications occurred in 27 (33.3%) patients ($\chi^2 = 10.9$, $p = 0.001$). Mortality was 4 (6.0%) and 2 (2.5%) respectively ($\chi^2 = 1.2$, $p = 0.3$).

In patients with sarcopenia infectious complications occurred in 7 cases, pancreatic fistula Grade B or C - in 22 patients, haemorrhage - in 9, delayed gastric emptying - in 2. In patients without sarcopenia infectious complications occurred in 6 patients, delayed gastric emptying - in 2, pancreatic fistula Grade B or Grade C in - 8 patients, haemorrhage - in 8, chyle leak - in 3.

We did not find any significant difference in the number of infectious complications ($\chi^2 = 0.2$, $p = 0.6$), delayed gastric emptying ($\chi^2 = 0.2$, $p = 0.7$) and haemorrhage ($\chi^2 = 0.4$, $p = 0.5$), but the level of pancreatic fistula Grade B or Grade C was significantly higher ($\chi^2 = 4.2$, $p = 0.04$) in patients with sarcopenia.

Discussion

The development of postoperative complications is a factor that significantly affects the course of the patient's disease [9]. The occurrence of postoperative complications often limits us in the timely administration of adjuvant chemotherapy. Predictability of the level of complications prior to surgery can potentially improve selection patients for surgery, especially in borderline resectable tumors.

TPI is a patient-specific measurement of muscle density and fatty infiltration that reflects the degree of sarcopenia. Sarcopenia is a secondary phenomenon in patients with pancreatic cancer and muscle tissue atrophy in the absence of necrosis with a decrease in size and number of muscle cells, which may be a reversible process.

Our results show that TPI is a reliable predictors of postoperative complications after pancreatic resection in patients with pancreatic cancer.

Patients with high level risk of complications may undergo neoadjuvant chemotherapy, receiving concomitant therapy to improve their sarcopenia profile (nutrition optimization and physical training) before radical surgery.

This approach can ultimately reduce the level of postoperative complications after pancreatic surgery, which will lead to a better outcome that can potentially change the prognosis of this disease [10-12].

The obtained results are clinically applicable to patients with malignant tumors who are candidates for radical pancreatic resection. In addition, sarcopenia is a condition of the body that can change over time. In the future, there is a need to develop a therapeutic strategy to increase the patient's muscle mass, positively change their sarcopenia profile and reduce the risk of postoperative complications.

According to Tosei Takagi and co-authors, sarcopenia is an objective and reliable preoperative predictor of postoperative infectious complications after pancreatic resection [13]. We have not received such data.

Yasunori Nishida showed a significant increase in the incidence of pancreatic fistulas after pancreatic resection in patients with sarcopenia. We received similar date [14]. According to the results of our research, the number of complications in patients with sarcopenia significantly increased, in particular the number of pancreatic fistula.

Determining the presence of sarcopenia can help surgeons to predict the occurrence of postoperative complications and influence the tactics of perioperative treatment. However, a therapeutic strategy for increasing lumbar mass and for improving sarcopenic profile to reduce the risk of complications remains to be developed.

Conclusion

The findings suggest that sarcopenia, determined by TPI in preoperative CT investigations is a significant indicator of surgical outcome and has a significant effect on the level of postoperative complications and can be used to improve patient selection before performing resection of malignancies.

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