Body Composition Assessment in Patients with Periampullary Neoplasma Undergoing Pancreaticoduodenetomy and its Predictive Value for Postoperative Complications

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Research Article

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Abstract

Background

To observe body composition parameters variance in patient with periampullary neoplasmas with different clinical characteristics and assess its predictive value for postoperative complications after pancreaticoduodenectomy.

Methods

In this study, we retrospectively reviewed the clinical and image data of 144 patients with periampullary neoplasmas.The area of subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT) and total abdominal muscle area (TAMA) were measured from preoperative CT images at the 3rd lumbar vertebra level, the TAMA was normalized to stature and termed as skeleton muscle index (SMI). The perioperative and pathological data were collected.

Results

Of the included 144 patients, 80(55.6%), 29(20.1%) and 24(16.7%) patients were classified as sarcopenia, visceral obesity and sarcopenic obesity. 84(58.3%) patients were jaundiced and 28 (19.4%)、50 (34.7%)、66(45.8%) patients were diagnosed with benign pancreatic tumors, pancreatic cancer and non-pancreatic cancer respectively. The incidence rate of clinical postoperative pancreatic fistula(POPF) and other major complications were 38.2% and 16%.In the univariate analysis, jaundiced patients experienced more weight loss and had higher nutrition risk score, the TAMA[103.1(61.1-176.7) vs 111.8(74.1-198.2),P=0.021] and SMI(39.2±7.0 vs 42.6±9.1,P=0.012)were lower compared with non-jaundiced group. However, no significant difference were founded between different pathological results and it was not associated with occurrence of POPF and major complications.

Conclusion

Jaundiced patients may experience more weight loss and have lower TAMA and SMI. Body morphometric analysis of preoperative CT did not show predictive value for postoperative complications and further multicenter studies are needed.

Trail registration

Registration number：2021-437-01.

Introduction

Incidence of biliopancreatic tumors is increasing year by year and pancreatic carcinoma shall be the second malignancy leading to death until 2030[1]. For the patients with periampullary neoplasmas such as pancreatic cancer, distal cholangiocarcinoma, duodenal tumors may firstly manifest as jaundice,

abdominal pain and gradually the lumen of duodenal will be obstructed, patients more or less may experience dyspesia and weight loss for digestion and absorption of food being influenced. Although great improvements have been achieved in oncological and endoscopic therapy, radical surgical resection is still the first choice[2]. Pancreaticoduodenectomy is the standard procedure for the treatment of periampullary tumors, while the high incidence of postoperative complication about 30%-50% not only affecting patients' recovery thus extended hospitalization but also delaying the time received adjuvant therapies[3–4].

Recently, reports have shown that preoperative body composition change can predict the surgical complication and survival of several malignant tumors, especially who are sarcopenic and visceral obesity[5–7]. Given the fact that patients with pancreatic cancer may experience exocrine insufficiency and sarcopenia is common[8–10], so we suppose that body composition change may have some relationship with postoperative complication. In this article ,we are aimed to analyze the change of body composition in patients with periampullary tumors and assess its value in predicting postoperative complications.

Materials And Methods

Patients

This retrospective studies were approved by the Health Research Ethics Board of Drum-Tower Hospital Affiliated to Nanjing University Medical School.Every patient had signed the informed consent. Patients had radiology-proven or pathology-diagnosed tumors in pancreatic head, distal biliary tract or duodenal wall and met the inclusion criteria below from December 2017 to January 2020 were included. All patients were successfully performed pancreaticoduodenectomy. The inclusion criteria were as follows: (a) patients who were treated with pancreatoduodenectomy for periampullary neoplasmas (b) patients without other active cancer; (c) patients > 18 years of age; and (d) patients who underwent preoperative enhanced CT within 1 month before operation. The exclusion criteria were as follows: (a) whose preoperative CT cannot be obtained with 1 month before operation;(b) whose clinical data are incomplete.

Acquisition and analysis of CT image

CT images were downloaded from the Picture Archiving and Communication System(PACS) of the Radiology Department including unenhanced-,artery- and portal venous phase of upper abdomen. Two radiologist(Shanshan Xu、Yifan Zhang)analyzed the images and calculated the areas using 3D Slicer software (v. 4.10.2, www.slicer.org) and the other physician(Jian He) checked the results, both of them were blinded to the patients' information. Different tissue were distinguished by specified Hounsfield Unit and area of SAT(HU:-190 to -30),VAT(HU:-150 to -50),TAMA(HU:-29 to +150)were measured at the 3rd lumbar vertebra level(L3)[11](Figure 1). The TAMA was normalized to stature by dividing the muscle area by the patient's height squared, and which is termed the skeletal muscle index (SMI= TAMA (cm^2)/height (m^2)).Sarcopenia was defined using SMI cut-off value:42.2cm^2/m^2 for men and 33.9cm^2/m^2 for

women[12]. Visceral obesity was defined as VFA > 136 cm^2 in men and > 95 cm^2 in women[13]. The cut-off value for diagnosing sarcopenic obesity was 3.2(VAT/SMI)[14].

Clinical data collection and definition of complication

Clinical data were collected including demographics(age, sex, pre-hospitalization weight loss, history of diabetes),preoperative nutrition risk score(NRS-2002,PG-SGA),preoperative laboratory data(hemoglobulin, transaminase, total bilirubin, albumin, prealbumin, C reactive protein),data of surgery(type of surgical procedure, length of operation volume of blood loss and transfusion),pathologic results. Postoperative complications included clinical pancreatic fistula(Grade B/ C) and surgery-related complications classified by the Clavien–Dindo classification, with major complications defined as grade ≥[15-16].

Statistics

Statistical analysis was performed using SPSS 23.0 software (SPSS Inc.). Measurement data with normal distribution were presented as mean and standard deviation, and comparison between groups was analyzed using independent t test. Measurement data with skewed distribution were described as median(range),and comparison between groups was analyzed using Mann-Whitney U test. Count data were expressed as absolute number and percentage, and comparison between groups was analyzed using c^2 test. Univariate analysis was conducted using the c^2 test. $P<0.05$ was considered as statistics significantly.

Results

Study cohort

In this study,144 patients met the criteria above were included. The group consisted of 88(61.1%) men and 56(38.9%) women, the average age was 62.4±12 years old. When admitted to hospital,84(58.3%) patients were classified into jaundice group whose total bilirubin level ≥34.2μmol/L. According to the sex-specific cut-off value,80(55.6%)patients were defined as being sarcopenic. Visceral obesity was observed in 29(20.1%)patients. When combined the two factors together, 24(16.7%)patients were diagnosed as sarcopenic obesity. All patients were performed pancreaticoduodenectomy successfully, 55(38.2%)patients developed clinical pancreatic fistula and 23(16%)patients developed major postoperative complications(Calvin-Dindo grade≥). In the 144 patients,28(19.4%)of them were diagnosed with pancreatic benign tumors,50(34.7%) and 66(45.8%) patients were diagnosed with pancreatic cancer and non-pancreatic cancer including distal cholangiocarcinoma, duodenal cancer, ampullary carcinoma respectively.

Comparison of body composition according to preoperative bilirubin level

The clinical characteristic between jaundiced and non-jaundiced patients were listed on Table 1 .Beside the variables reflects liver function were higher in jaundice group, more weight loss and higher nutrition risk score were founded compared with non-jaundiced group. The average TAMA and SMI were lower and VAT/TAMA ratio was higher in jaundiced group. Gender, BMI, SAT, VAT , rates of sarcopenia, visceral obesity and sarcopenic obesity showed no difference between the two groups.

Table 1 Comparsion between jaundiced and non-jaundiced patients

Clincal data	Jaundice（n=84）	Non-jaundice（n=60）	P value
Age	65（32-82）	62（20-82）	0.03
Gender（M/F）	52/32	36/24	0.817
Weight loss（Kg）	4（0-30）	2.5（0-15）	0.026
NRS-2002 score	4（0-6）	4（0-6）	0.009
PG-SGA score	10（3-20）	6（1-18）	0.001
BMI（kg/m^2）	22.6（15.6-41.1）	23.3（16.5-31.6）	0.884
ALT（U/L）	171.9（23.9-688.9）	20.5（3.3-432.6）	0.001
AST（U/L）	120.6（18.7-538.7）	21.3（6.3-235.8）	0.001
TB（μmol/L）	168.8（43.9-524.7）	10.7（3-34）	0.001
DB（μmol/L）	120.4（28.2-319.4）	2.5（0.8-23.3）	0.001
ALB（g/L）	36.9（24.2-42.5）	39.9（30.5-45.4）	0.001
Pro-Alb（g/L）	140.6±52.1	197.5±61.5	0.001
C reactive protein	8.3（0.8-135）	4.6（1.5-114.4）	0.001
Diameter of MPD（mm）	3（1-15）	3 （1-25）	0.334
SAT（cm^2）	97.7（28.7-259.9）	105.6（32.1-194.8）	0.795
VAT（cm^2）	85.2±47.6	78.6±49.6	0.422
TAMA（cm^2）	103.1（61.1-176.7）	111.8（74.1-198.2）	0.021
SMI（cm^2/m^2）	39.2±7.0	42.6±9.1	0.012
VAT/TAMA	2.18±1.19	1.79±1.02	0.043
Sarcopenia	52（61.9%）	28（46.7%）	0.07
Visceral obesity	19（22.6%）	10（16.7%）	0.38
Sarcopenic obesity	14（16.7%）	10（16.7%）	1.0

*BMI：body mass index; Hb:hemoglobin ;ALB:albumin;SAT:subcutaneous adipose tissue;VAT:visceral adipose tissue;TAMA:total abdominal muscle area;SMI:skeleton muscle index

Comparison of body composition according to pathologic results

The 144 patients enrolled in this study were classified into three groups as benign tumor group, pancreatic cancer(PC)group, non-pancreatic cancer group(Non-PC)according to the pathological result of the specimen. When compared the clinical data of these groups together as shown in Table 2 , only gender, serum bilirubin level and pro-albumin concentration showed statistical difference, while age, BMI, nutrition risk score, body composition parameters(SAT,VAT,TAMA,SMI)did not show any significant difference.

Table 2 Comparsion of clinical characteristics according to different pathologic results

Clincal data	Benign Tumor	PC	Non-PC	P value
Age	65（20-77）	62（32-82）	64（36-82）	0.111
Gender（M/F）	13/15	37/13	38/28	0.041
Weight loss（Kg）	2.5（0-15）	4（0-30）	3（0-15）	0.46
NRS-2002 score	3（0-6）	4（0-6）	4（0-6）	0.501
PG-SGA score	5.5（2-17）	9.5（2-20）	9.5（1-19）	0.389
BMI（kg/m^2）	23.3（17.7-28.4）	23.2（16.5-31.2）	22.6（15.6-41.1）	0.599
ALT（U/L）	20.5（3.3-452.8）	125.8（8.3-688.9）	134.5（7.9-454.1）	0.087
AST（U/L）	23.5（6.3-359.9）	88.7（9.5-454.2）	96（8.5-538.7）	0.053
TB（μmol/L）	10.1（3-137.9）	113.4（4.3-413.8）	141.9（5.9-524.7）	0.049
DB（μmol/L）	2.3（1-99.2）	85.1（0.8-287.7）	107.9（0.8-319.4）	0.038
ALB（g/L）	40（33.1-44）	38.5（29.4-45.4）	36.8（24.2-42.2）	0.036
Pro-Alb（g/L）	193.3±65.6	163.2±53.6	152.8±64.7	0.008
C reactive protein	4.8（1.7-114.4）	5.3（1.5-102.7）	7.2（0.8-135）	0.299
Diameter of MPD（mm）	3（1-25）	4（1-15）	3（1-12）	0.38
SAT（cm^2）	86.8（34.5-194.8）	109.1（28.7-259.9）	99.2（29.6-236.8）	0.565
VAT（cm^2）	74.1±51.9	79.4±46.2	88.3±48.4	0.149
TAMA（cm^2）	113.7（75.1-172.9）	101.4（71.9-198.2）	107.1（61.1-163）	0.159
SMI（cm^2/m^2）	42.4（29.1-63.5）	38.5（27.2-71.9）	40.1（25.4-57.6）	0.233
VAT/TAMA	1.67±0.99	2.21±1.22	2.03±1.11	0.141
Sarcopenia	17（60.7%）	25（50%）	38（57.6%）	0.596
Visceral obesity	2（7.1%）	11（22%）	16（24.2%）	0.154
Sarcopenic obesity	3（10.7%）	8（16%）	13（13.7%）	0.558

PC: pancreatic carcinoma; Non-PC including distal cholangiocarcinoma, cancer of ampulla and duodenal carcinoma.

Analysis of related variables of postoperative complications

In the univariate analysis, several related factors that may predict POPF and major complication are shown in Table 3 and Table 4. Between patients with and without POPF, only the diameter of MPD

showed difference significantly. Between patients with and without major complications, only the pre-operative WBC counts differed significantly. Contrary to our previous hypothesis, body composition parameters(SAT,VAT,TAMA,SMI)did not show any value in predicting POPF and major complications.

Table 3 univariate analysis of potential factors associated with POPF

	POPF（grade B/C）		P value
Clinical data	With POPF（n=55）	Without POPF（n=89）	
Age	64.5（31-82）	65（20-82）	0.492
Gender（M/F）	33/22	55/34	0.83
Weight loss（Kg）	3（0-15）	3（0-30）	0.417
NRS-2002 score	4（0-6）	4（0-6）	0.409
PG-SGA score	8（2-20）	9（1-17）	0.544
BMI（kg/m^2）	23.7±3.6	22.9±3.2	0.156
WBC（$\times10^9/L$）	5.8±1.9	5.6±1.9	0.521
Hb（g/L）	122.2±18.1	122.3±15.6	0.969
Plt（$\times10^9/L$）	222（84-436）	215（55-516）	0.474
ALB（g/L）	37.9（25.6-44）	38（24.2-45.4）	0.844
Pro-Alb（g/L）	166.8±70.5	162.8±57.7	0.711
C reactive protein	5.5（0.8-135）	5.4（1.3-113.4）	0.577
SAT（cm^2）	102.7（35.5-236.8）	99.3（28.7-259.9）	0.623
VAT（cm^2）	88.6±47.2	78.7±48.9	0.235
TAMA（cm^2）	107.3±27.2	110.6±25.3	0.472
SMI（cm^2/m^2）	39.8±8.4	41.2±7.8	0.31
VAT/TAMA	2.25±1.21	1.89±1.08	0.065
Sarcopenia	34（61.8%）	46（51.7%）	0.234
Visceral obesity	9（16.3%）	20（22.5%）	0.375
Sarcopenic obesity	5（9.1%）	19（21.3%）	0.055
Diameter of MPD（mm）	3（1-8.6）	4（1-25）	0.027
Length of operation（min）	367.5（230-800）	380(225-745)	0.866
Blood loss（ml）	450（100-3600）	500（50-3200）	0.404
Blood transfusion（ml）	0（0-4100）	0（0-1925）	0.866

Table 4 univariate analysis of potential factors associated with major complications

	Major complications（Calvin-Dindo grade≥3）		P value
Clinical data	with（n=23）	without（n=121）	
Age	64（44-80）	65（20-82）	0.902
Gender（M/F）	17/6	71/50	0.169
Weight loss（Kg）	3（0-15）	3（0-30）	1.0
NRS-2002 score	4（0-6）	4（0-6）	0.282
PG-SGA score	8（2-19）	9（1-20）	0.522
BMI（kg/m^2）	23.3±3.1	23.1±3.4	0.891
WBC（$\times10^9/L$）	6.3（3.3-10.2）	5.1（2.4-12.3）	0.015
Hb（g/L）	124.5±19.1	121.9±16.1	0.486
Plt（$\times10^9/L$）	232（91-422）	215.5（59-516）	0.256
ALB（g/L）	36.7（25.6-44）	37.9（24.2-45.4）	0.561
Pro-Alb（g/L）	166.6±77.1	163.8±59.9	0.845
C reactive protein	5.5（0.8-84）	5.4（1.3-135）	0.733
SAT（cm^2）	103.1（29.6-188.2）	98.7（28.7-259.9）	0.653
VAT（cm^2）	82.9±52.9	82.4±47.7	0.956
TAMA（cm^2）	101.2（72.5-172.9）	107.3（61.1-198.2）	0.705
SMI（cm^2/m^2）	40.3±9.6	40.7±7.8	0.805
VAT/TAMA	2.15±1.52	2.0±1.05	0.56
Sarcopenia	15（65.2%）	65（53.7%）	0.309
Visceral obesity	3（13%）	26（21.5%）	0.57
Sarcopenic obesity	1（4.3%）	23（19%）	0.125
Diameter of MPD（mm）	3（1-8.6）	3（1-25）	0.943
Length of operation（min）	395.2±122.1	391.6±98.9	0.878
Blood loss（ml）	500（100-3600）	400（50-3200）	0.585
Blood transfusion（ml）	300（0-3375）	0（0-4100）	0.374

Discussion

In this retrospective study, it revealed that jaundiced patients with periampullary tumors is more prone to loss weight and have higher nutrition risk scores. when introduced CT images as an evaluation modality, it showed significant difference between jaundice and non-jaundice patients in TAMA and SMI. While morphometric parameters such as sarcopenia and visceral obesity were not predictive factors of POPF and other major complications after pancreaticoduodenectomy.

Recent years, the incidence of biliopancreatic carcinoma is increasing and surgical resection still remains the curative therapy. Nevertheless, the high incidence of morbidity and mortality about 40% and 5% respectively threaten patients' recovery. It had been thought that perioperative management and the TNM-stage of tumor were vital factors affected the recovery and prognosis[17–18], but it is gradually drawing attention that patient individual characteristic such as combined-disease, nutritional status may play an important role as well. BMI, nutrition risk score(NRS-2002,PG-SGA score) are the common nutrition appraisal tools, but BMI reflects the overall nutrition status and might cause some bias. For example, an obese patient may have excessive adipose accumulation while the muscle may atrophy or be infiltrated by fat[19–20]. Our institution also conducted body composition analysis by bioelectrical impedance(BIA), but the result maybe inconsistent[21–22]. Nowadays, CT acts as a new tool assessing the body composition is gaining its popularity for its accuracy and reliability[23]. Several study on hepatocellular carcinoma, gastric and colorectal carcinoma showed that preoperative sarcopenia and visceral obesity have significant impact on postoperative complication and overall survival rate[6, 24].

Jaundice is the common symptom of bilio-pancreatic disease for the outlet of the bile tract is obstructed, dyspepsia and weight loss were general complaints of these patients as well. Clugston et al's [25]study showed that jaundiced group were significantly malnourished and thus the surgery-related mortality and duration of stay after intervention were differed from non-jaundiced group, which was similar to our results in some extents. We further evaluated the nutrition status of the included patients according to the area of muscle and adipose tissue at the L3 vertebral body level. The TAMA and SMI were higher in non-jaundiced group and was consistent with its higher nutrition risk score. Several points may account for it. First of all, bile is an important substance to promote fat digestion, insufficient production of bile can lead to steatorrhea and vitamin deficiency[26]. Secondly, dysfunction of kupffer cell, proliferation and translocation of gut normal bacterium and accumulation of bacterium in bile make the body be in inflammatory state and prone to suffer from cholangitis, which leads to the increased consumption of protein[27–28]. Last but not least, impaired hepatocellular function results in insufficient protein synthesis, gluconeogenesis, and ketogenesis disorders[29]. Although there is no consensus on routine biliary drainage before operation, it is wise to adopt biliary drainage and reuse to maintain the normal enterohepatic circulation in malnourished patients and morphometric parameters from CT images could be a reference.

When the body composition parameters of three different pathologic types of periampullary tumors classified as benign tumors, pancreatic carcinoma and non-pancreatic carcinoma were compared, no significant difference were observed. Pancreas is the exocrine organ of great importance through

secreting several enzymes assisting the digestion, and more than 50% of patients with pancreatic ductal carcinoma suffered from weight loss compared to the percentage about 10% in ampullary cancer group[30–31]. Causes of high incidence of weight loss in pancreatic carcinoma group can be attributed to tissue-fibrosis, exocrine and endocrine insufficiency, obstruction of duodenum and cancer induced cachexia[32–33]. Contrary to the original hypothesis, patients with resectable pancreatic carcinoma experienced less muscle loss compared with unresectable or borderline resectable group, which had been indentified in Sandini et al's study that loss of muscle tissue is associated with tumor resectability[34].

In the univariate analysis ,diameter of MPD is the only factor associated with POPF which has been validated in previous study[35]. However, out of expectation, we did not find sarcopenia, visceral obesity and sarcopenic obesity impact the morbidity. It was doubtful that whether sarcopenia relate to the POPF. Kosei et al's[36] study showed that sarcopenia was the risk factor of postoperative infectious complications for the cancer impaired immune function, but more research insisted that sarcopenia alone may not predict the clinical outcome in that it only reflects the depleted mass not the quality of muscle[37–38]. A clinical prospective study conducted by Huang et al proposed sarcopenia should be defined as low muscle mass, low strength and physical performance[39].In their results, low muscle mass(OR 3.853, 95% CI 1.446–10.263, P = 0.007)(be regarded as sarcopenia in most study)and sarcopenia(OR 4.758, 95% CI 1.627–13.917, P = 0.004)were independent risk factors for the postoperative morbidity, while sarcopenia had better predictive power when the two functional tests were added.

It had been identified in a series of studies that excessive visceral not subcutaneous adipose tissue was the risk factor of postoperative morbidities. On the one hand, increased adipose mass may add extra difficulties to the operation[41–42], on the other hand, visceral adipose tissue is considered to be an active organ producing some cytokines and pro-inflammatory adipocytokines such as leptin, TNF-α, IL-1, and IL-6 leading to the delayed healing of wound especially the pancreaticoenteric anastomosis[43–45]. Nevertheless, The results of this study were inconsistent with our expectations that visceral obesity or sarcopenic obesity did not impact the outcome. It can be attributed to the indefinite cutoff point of visceral obesity and sarcopenic obesity between different population or nations, so further studies need to be conducted[46].

The present study has various limitations. First, it was a retrospective study based on available data, so we can not evaluate the function of muscle such as handgrip strength and 6-m usual gait speed, which was adopted in limited research and further prospective studies of functional tests ought to be conducted. Second, the study was a small study from a single center, to validated the value of body composition parameters on complications, multicenter researches are indispensable.

In conclusion, the results of our study showed that jaundiced patients may experience more weight loss in the early stage of disease, while the parameters of body composition such as sarcopenia and visceral

obesity did not show significant predictive value on postoperative complications and further multicenter studies are needed.

Abbreviations

SAT:subcutaneous adipose tissue;VAT: visceral adipose tissue ;TAMA:total abdominal muscle area;SMI:skeleton muscle index;POPF:postoperative pancreatic fistula;BMI：body mass index; Hb:hemoglobin ;ALB:albumin;PC: pancreatic carcinoma.
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Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (*Trial registration number：2021-437-01*).Every patient had signed the informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from YD Qiu and J He on reasonable request.

Competing interests

The authors declare that they have no conflict of interest.

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Authors' contributions

QYD and HJ contributed to the conception of the study.XSS and ZYFconducted the CT image analysis and checked by HJ.YYF contributed to the data analysis.CZH performed the data analysis and wrote the manuscript.

All authors have read and approved the manuscript.

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Figures

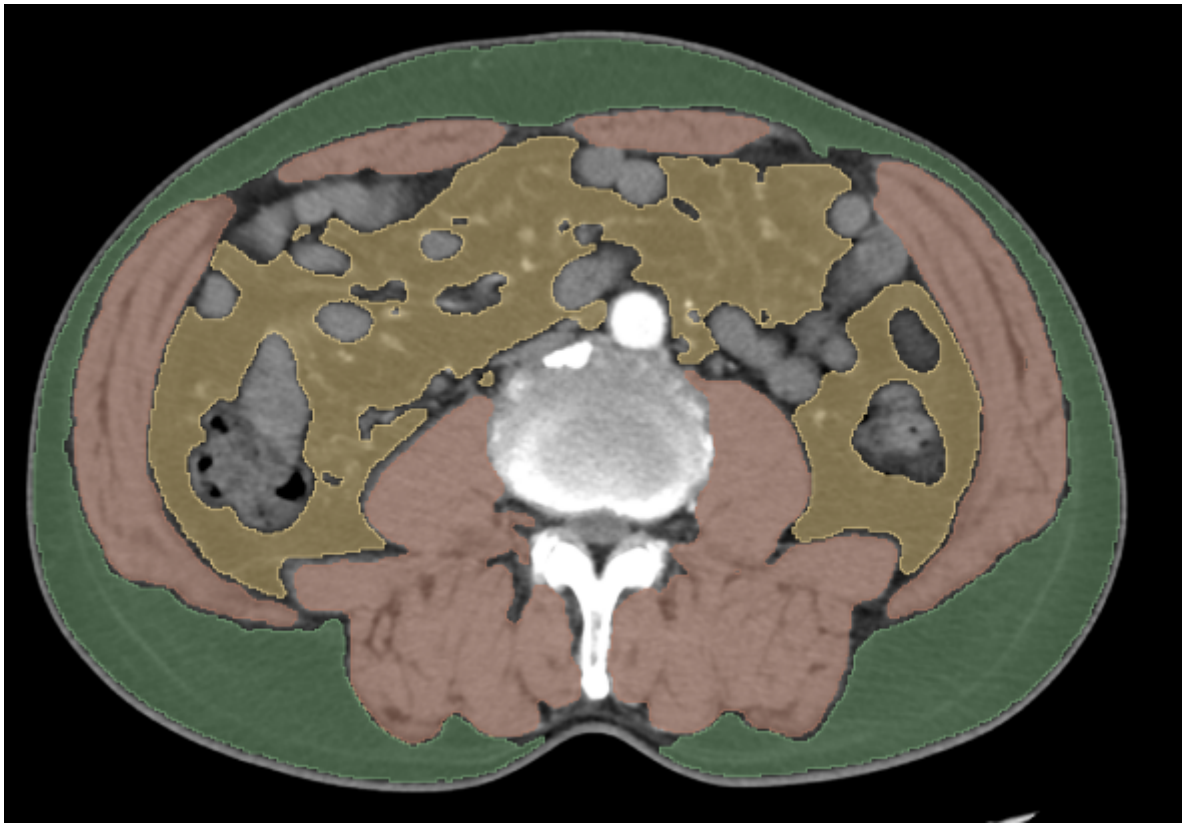

Figure 1

Body composition measurement based on CT image, areas of green, yellow and red represent subcutaneous adipose tissue, visceral adipose tissue and skeleton muscle respectively.