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Contents

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LETTER TO THE EDITOR

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AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 1375 experts in gastroenterology and hepatology from 68 countries.

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ORIGINAL ARTICLE

Observational Study

Consequences of metabolic syndrome on postoperative outcomes after pancreaticoduodenectomy

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Abstract

AIM

To analyze immediate postoperative outcomes after pancreaticoduodenectomy regarding metabolic syndrome.

METHODS

In two academic centers, postoperative outcomes of patients undergoing pancreaticoduodenectomy from 2002 to 2014 were prospectively recorded. Patients presenting with metabolic syndrome [defined as at least three criteria among overweight (BMI $\geqslant$ 28 kg/m^2), diabetes mellitus, arterial hypertension and dyslipidemia] were compared to patients without

metabolic syndrome.

RESULTS

Among 270 consecutive patients, 29 (11%) presented with metabolic syndrome. In univariable analysis, patients with metabolic syndrome were significantly older (69.4 years *vs* 62.5 years, $P = 0.003$) and presented more frequently with soft pancreas (72% *vs* 22%, $P = 0.0001$). In-hospital morbidity (83% *vs* 71%) and mortality (7% *vs* 6%) did not differ in the two groups so as pancreatic fistula rate (45% *vs* 30%, $P = 0.079$) and severity of pancreatic fistula ($P = 0.257$). In multivariable analysis, soft pancreas texture ($P = 0.001$), pancreatic duct diameter < 3 mm ($P = 0.025$) and BMI > 30 kg/m² ($P = 0.041$) were identified as independent risk factors of pancreatic fistula after pancreaticoduodenectomy, but not metabolic syndrome.

CONCLUSION

In spite of logical reasoning and appropriate methodology, present series suggests that metabolic syndrome does not jeopardize postoperative outcomes after pancreaticoduodenectomy. Therefore, definition of metabolic syndrome seems to be inappropriate and fatty pancreas needs to be assessed with an international consensual histopathological classification.

Key words: Soft pancreas; Postoperative outcomes; Metabolic syndrome; Pancreaticoduodenectomy

Core tip: As metabolic syndrome is related to fatty pancreas and fatty pancreas is related to pancreatic fistula, postoperative morbi-mortality should theoretically increase in patient with metabolic syndrome and undergoing pancreaticoduodenectomy. In two academic centers, postoperative outcomes of 270 consecutive patients undergoing pancreaticoduodenectomy were retrospectively compared in regards of metabolic syndrome. In multivariable analysis, soft pancreas texture ($P = 0.001$), pancreatic duct diameter < 3 mm ($P = 0.025$) and BMI > 30 kg/m² ($P = 0.041$) were identified as independent risk factors of pancreatic fistula after pancreaticoduodenectomy, but not metabolic syndrome. The present series suggests that metabolic syndrome does not jeopardize postoperative outcomes after pancreaticoduodenectomy.

Zarzavadjian Le Bian A, Fuks D, Chopinet S, Gaujoux S, Cesaretti M, Costi R, Belgaumkar AP, Smadja C, Gayet B. Consequences of metabolic syndrome on postoperative outcomes after pancreaticoduodenectomy. *World J Gastroenterol* 2017; 23(17): 3142-3149 Available from: URL: http://www.wjgnet.com/1007-9327/full/v23/i17/3142.htm DOI: http://dx.doi.org/10.3748/wjg.v23.i17.3142

INTRODUCTION

In spite of recent advances in pancreatic surgery, pancreaticoduodenectomy (PD) is still seen as a demanding procedure, ideally performed by experienced teams in high volume centres[1]. Indeed, when a decrease in postoperative mortality after PD has been observed over the last decades, it has not been associated with a similar reduction in morbidity rate that still ranges from 30% to more than 70%. Still, PD represents nowadays the main curative option for lesion located in the pancreatic head. Pancreatic fistula (PF) is the most common complication following PD and is responsible for a significant mortality and morbidity[2]. An extensive literature analysis identified several preoperative risk factors such as fatty pancreas infiltration, intra-abdominal obesity, all possibly related to metabolic syndrome (MS).

MS is defined by the association of three criteria among increased waist circumference or overweight/obesity, arterial hypertension, decreased serum HDL cholesterol, increased serum triglycerides and diabetes mellitus (DM) or increased fasting glucose[3]. With a rising incidence[4], it has become a contemporary concern. Yet, MS has been linked to fatty pancreas when obesity is involved[5] and fatty pancreas is also associated with DM (without MS)[6]. Interestingly, fatty pancreas and increased body mass index (BMI) are associated with increased rate of pancreatic fistula (PF)[7-9]. Additionally, both impaired performance status of these patients as a consequence of advanced age, central obesity, diabetes mellitus and cardiovascular co-morbidities, as well as the impact of the underlying liver status, may have impact after pancreatic surgery. Therefore, theoretically, MS could adversely affect the postoperative course in patients undergoing PD. These issues are still largely unclear and currently, only one study has analyzed the influence of MS on postoperative outcomes in pancreatectomy[10], showing increased postoperative morbidity.

Therefore, the present series aimed to characterize the outcomes in MS patients who underwent PD in order to determine the influence of the MS on the postoperative course.

MATERIALS AND METHODS

Patient's selection

From February 2002 to December 2014, data of all consecutive patients undergoing PD at Institut Mutualiste Montsouris (Paris, France) and Hôpital Antoine Béclère (Clamart, France) were retrieved from a prospectively collected database. Surgical approach and pancreatic reconstruction [pancreaticojejunostomy (PJ) or pancreaticogastrostomy (PG)] was left to the surgeon's discretion. The diagnosis of MS was considered when three or more of the following criteria were present[3]: central obesity; dyslipidemia

(triglycerides 1.7 mmol/L or above, or high-density lipoprotein cholesterol less than 1.03 mmol/L in men or less than 1.29 mmol/L in women); type Ⅱ diabetes or glucose intolerance with fasting glucose 5.6 mmol/L or above; and arterial hypertension (blood pressure above 135/85 mmHg). Because of the retrospective nature of the study, it was assumed that central obesity was reached when the patient's body mass index was greater than 28 kg/m² (as normal WHO BMI < 25 kg/m²[11]), that patients receiving statin or fenofibrate medication had dyslipidemia, that patients treated for hypertension had arterial hypertension. In spite of recent results[12], level of serum uric acid was not considered as it was not routinely performed.

Preoperative evaluation and postoperative outcomes

Preoperative investigations included complete blood tests as well as routine cardiorespiratory evaluation. Computed tomography and/or magnetic resonance imaging were performed to assess tumor characteristics.

All resections were performed with curative intent. All intraoperative parameters, including blood loss with subsequent blood transfusion and duration of surgery, were recorded. The pancreatic parenchyma consistency, soft or hard, was evaluated intraoperatively by the surgeon by manual palpation of the pancreatic remnant. Pancreatic duct diameter was measured using a scale.

Postoperative complications were stratified according to the Clavien-Dindo classification[13], which defines major complications by a score of 3 or more. Specific pancreatic complications were detailed as follows: PF was defined according to the ISGPF definition[14]; haemorrhage was defined as a drop of haemoglobin level > 3 g/dL after the end of surgery compared to postoperative baseline level and/or any postoperative transfusion of packed red blood cell units for a falling haemoglobin and/or the need for invasive re-intervention[15] and biliary leakage was defined by a bilirubin concentration in the drainage fluid more than threefold higher than that in serum[16]. Both complications and operative mortality were considered as those occurring within 90 d of surgery, or at any time during the postoperative hospital stay.

Statistical analysis

Patient baseline characteristics are expressed as median (range) for continuous data, and as numbers with percentages for categorical data. Fisher's exact test was used to compare differences in categorical variables, and the Wilcoxon rank sum test for continuous variables. Variables achieving statistical significance at the 0·1 level in univariable analysis were considered for multivariable analysis. A backward variable procedure was used to identify independent predictive factors. A *P* value of 0.05 was considered statistically significant and odds ratios (OR) with 95%CI were calculated. All statistical analyses were performed with PASW (SPSS) 18.0 (SPSS Inc, Chicago, IL, United States).

RESULTS

Patients' characteristics

From 2002 to 2014, 270 patients underwent PD. There were 169 (63%) males with a median age of 64.5 years (range 30.6-88.7). Among these patients, 29 (11%) were diagnosed with MS, defining the MS group. Patients' characteristics depending on MS are detailed in Table 1.

MS patients were significantly older (69.4 years *vs* 62.5 years, *P* = 0.003) than non-MS patients. MS group presented more frequently with jaundice (31% *vs* 20%, *P* = 0.004) and required biliary stenting more often than the Non-MS group (59% *vs* 34%, *P* = 0.008). Tumor characteristics (such as indications for PD)(Table 1) and indication for neoadjuvant treatment were comparable in the two groups.

Surgical procedures

Intraoperative blood loss, operative time and resection of adjacent organ were similar in both groups (Table 2). In 65 (24%) patients, the PD was completed laparoscopically. Resection of the portal vein was required in 44 (16%) patients. During surgical examination, soft pancreatic parenchyma was more frequently observed in patients with MS (72% *vs* 22%, *P* = 0.0001). Pancreaticogastrostomy (PG) and pancreaticojejunostomy (PJ) were performed in 109 (40%) and 161 (60%) patients, respectively, with no difference in the two groups.

Pathology and postoperative outcomes

Among 232 (86%) patients who underwent PD for malignancy, R0 resection was achieved in 183 (79%) patients with no difference between the two groups. Seventeen (6%) patients died during the early postoperative period, three had MS. Postoperative complications are detailed in Table 3. Statistical analysis revealed no significant difference between MS and Non-MS groups regarding overall (*P* = 0.195), minor (*P* = 0.639) and major (*P* = 0.123) complications. Pancreatic fistula and its severity were comparable in the two groups even though there was a non-significant tendency towards higher PF in the MS group. Multivariate analysis (Table 4) demonstrated soft pancreas texture (*P* = 0.001), pancreatic duct diameter < 3 mm (*P* = 0.025) and BMI > 30 kg/m² (*P* = 0.041) as independent risk factors however MS was not. Delayed gastric emptying and haemorrhage rate were comparable in the two groups. Overall, median in-hospital stay reached 23 d with no difference in the two groups.

DISCUSSION

This study has been initially designed from a simple

Table 1 Demographic characteristics *n* (%)

	Non-MS group (*n* = 241)	MS group (*n* = 29)	*P* value
Preoperative characteristics			
Male gender	148 (61)	21 (72)	0.170
Age (yr), mean (range)	62.5 (30.6-88.7)	69.4 (52.1-80.3)	0.003
> 75 yr	8 (28)	42 (17)	0.141
ASA score ⩽ 2	204 (85)	22 (76)	0.171
Median BMI (kg/m^2)	23.5	27.2	0.001
> 30 kg/m^2	11 (5)	6 (21)	0.0001
Diabetes	26 (11)	18 (62)	0.0001
Hypertension	66 (28)	28 (97)	0.0001
Dyslipidemia	33 (14)	25 (86)	0.0001
Cardio-respiratory comorbidity			
Coronary heart disease	17 (7)	4 (14)	0.181
COPD	7 (3)	1 (3)	0.608
Alcohol	34 (14)	3 (10)	0.401
Tobacco	45 (19)	3 (10)	0.190
Initial presentation			
Jaundice	47 (20)	9 (31)	0.004
Biliary stenting	80 (34)	17 (59)	0.008
Abdominal pain	74 (31)	4 (14)	0.179
Baseline CA 19-9, mean (range)	312.8 (0-5300)	430.4 (35.2-1054)	0.710
Tumor diameter > 30 mm	80 (34)	6 (21)	0.838
Indications			
Malignant disease	211 (86)	27 (93)	0.516
Adenocarcinoma	141 (59)	17 (59)	0.842
Malignant ampuloma	25 (10)	2 (7)	0.557
Cholangiocarcinoma	21 (9)	5 (17)	0.142
Endocrine tumor	10 (4)	2 (7)	0.499
Other	14 (6)	1 (3)	0.148
Benign disease	30 (12)	2 (7)	0.385
IPMN	22 (9)	1 (3)	0.302
Other	8 (3)	1 (3)	0.742

MS: Metabolic syndrome; ASA: American society of anesthesiologists; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; IPMN: Intraductal papillary mucinous neoplasm.

Table 2 Intraoperative characteristics *n* (%)

	Non-MS group (*n* = 241)	MS group (*n* = 29)	*P* value
Soft pancreatic texture	53 (22)	21 (72)	0.0001
Pancreatic duct diameter < 3 mm	84 (35)	13 (45)	0.295
Vein resection	39 (16)	5 (17)	0.560
Visceral resection	21 (9)	3 (10)	0.490
Median surgery duration (mn)	430	462	0.285
Median blood loss (mL)	400	600	0.287
Perioperative transfusion	16%	29%	0.002

MS: Metabolic syndrome.

statement: because of demonstrated links between MS/obesity/DM[3,5-7] and fatty pancreas, and between fatty pancreas/obesity and PF after PD[7-9], common sense compels to guess that MS should be related to an increased rate of PF after PD. Also, as PF is also related to increased in-hospital mortality[17], the question of the link between MS and perioperative mortality seems pertinent. Regarding these queries, conclusions of this study may lead to change pre-operative and intraoperative managements in patients presenting with MS like previous studies have changed management in liver resection[18].

First, and considering pancreatic texture, soft pancreas (at intraoperative evaluation) has been previously related to fatty pancreas[19] and obesity[20]. In this analysis, soft pancreas, pancreatic duct diameter < 3 mm and obesity (BMI > 30 kg/m²) are demonstrated as independent risk factors of PF. Such results are in accordance with previous reports[7-9,21,22] and consequently are strengthening the background, coherence and methodology of this study. Indeed, compared to fatty pancreas as a predictive criterion (an histopathological finding requiring the specimen and available at least one week after the procedure), BMI can be assessed in the clinic, soft pancreas and duct dilatation are defined during the surgical procedure,

Table 3 Postoperative outcomes *n* (%)

	Non-MS group (*n* = 241)	MS group (*n* = 29)	*P* value
Postoperative complications	170 (71)	24 (83)	0.195
Clavien I-II complications	77 (32)	9 (31)	0.639
Clavien III-IV complications	78 (32)	12 (41)	0.123
Postoperative mortality	15 (6)	2 (7)	0.302
Pancreatic fistula	72 (30)	13 (45)	0.079
Grade of pancreatic fistula			0.257
A	16 (22)	4 (31)	
B	22 (31)	5 (38)	
C	34 (47)	4 (31)	
Delayed gastric emptying	12 (5)	1 (3)	0.583
Abdominal collection	54 (22)	7 (24)	0.496
Haemorrhage	44 (18)	6 (21)	0.800
Biliary fistula	16 (7)	1 (3)	0.762
Gastroenteric anastomosis fistula	5 (2)	1 (3)	0.814
Pulmonary complications	35 (15)	8 (28)	0.057
Reoperation	59 (24)	5 (17)	0.921
Hospital stay (d), median	22	25	0.972

MS: Metabolic syndrome.

Table 4 Risk factors of pancreatic fistula *n* (%)

	No pancreatic fistula (*n* = 185)	Pancreatic fistula (*n* = 85)	Univariate analysis	Multivariable analysis		
			P value	HR	95%CI	*P* value
Preoperative characteristics						
Male gender	108 (58)	61 (72)	0.023	1.45	0.038-9.204	0.418
Age > 75 yr	33 (18)	17 (20)	0.394			
ASA score ⩽ 2	161 (87)	65 (76)	0.125			
BMI > 30 kg/m^2	6 (3)	11 (13)	0.005	2.02	1.034-3.284	0.041
Diabetes	33 (18)	11 (13)	0.193			
Hypertension	57 (31)	37 (44)	0.041	1.03	0.005-14.58	0.250
Dyslipidemia	33 (18)	25 (29)	0.132			
Metabolic syndrome	16 (9)	13 (15)	0.137			
Coronary heart disease	10 (5)	11 (13)	0.049	3.51	0.108-2.071	0.865
COPD	7 (4)	1 (1)	0.443			
Alcohol	21 (11)	16 (19)	0.083	0.25	0.024-3.578	0.725
Tobacco	28 (15)	20 (23)	0.125			
Malignant disease	165 (89)	73 (86)	0.825			
Surgical procedures						
Pancreatogastrostomy	76 (41)	33 (39)	0.893			
Soft pancreatic texture	42 (23)	32 (38)	0.001	3.37	1.124-3.217	0.001
Pancreatic duct diameter < 3 mm	55 (30)	42 (49)	0.003	1.45	1.045-2.452	0.025
Vein resection	38 (20.5)	6 (7.0)	0.002	2.25	0.045-4.393	0.486
Arterial resection	2 (1.0)	0 (0)	0.925			
Visceral resection	17 (9)	7 (8)	0.499			
Perioperative transfusion	27 (15)	14 (16)	0.528			

MS: Metabolic syndrome; ASA: American society of anesthesiologists; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease.

enabling to modify the surgical strategy and to adapt the postoperative management. Interestingly, due to the subjectivity of evaluation (depending on the surgeon), soft pancreas texture may be argued as being unreliable. Also and considering PF, no other independent risk factor was identified, including DM and MS.

Regarding the influence of MS on PF and post-operative mortality, no link was demonstrated in this study. So far, several studies evaluating individually components of MS (mainly DM and obesity) are well known but only one analysis regarding MS and pancreatic resection has been reported[10]. This previous report showed an increased morbidity (including severe morbidity, but without increased rate of PF) regarding all pancreatic resections[10]. Currently, in scientific literature, DM is demonstrated as being associated with soft pancreas[6] but not with an increased rate of PF in PD[23]. On the contrary, obesity has already been related to an increased risk of PF[7-9] and to soft pancreas[20]. Unfortunately, in all these studies MS was not evaluated as an independent risk factor. On the subject of postoperative mortality (and regardless PF), MS did not show any effect in this study. Because of MS

and potential frailties (DM, arterial hypertension and their vascular consequences), a higher mortality rate could have been expected in MS group. In accordance with such hypothesis, MS has been recently linked to postoperative mortality after various surgical procedures such as liver resections[17,24,25], vascular procedures[26] and urology[27], and is known to be responsible for reduced life expectancy[28]. Also, with a well-known link between PF and postoperative mortality in PD[17], an increased rate of PF related to MS in this study would have resulted in an increased mortality. The analysis has refuted this hypothesis. Comparison of the PF Grade according to ISGPF Classification did not show any difference as well. These results suggest that MS does not lead to major complications. Consequently, without increased rate of PF and postoperative mortality, MS should not be seen as a contraindication to perform a PD.

This study and its results are worth a commentary as it failed to reach significance in spite of a consistent reasoning. When methodology may be commented - this small sample was recorded during a decade and retrospectively analyzed -, results suggest it is appropriate. So, failure to reach significance (MS increasing PF and mortality) needs to be rationalized. As previously described, fatty pancreas, soft pancreas (evaluated and depending on surgeons), MS and its independent criteria (mainly obesity and DM) composed a group of interrelated affections. Considering PD, several reports have supported all these affections as being independent risk factors of PF (except DM that is not a risk factor of PF in spite of being a risk factor of fatty pancreas). Also, regarding influence of DM on PF, a recent meta-analysis[23] showed a protective effect of DM, with more fatty pancreas and soft pancreas in patients without DM. These results lead to two remarks. First, when the targeted disease is insulin resistance, definition of MS does not discriminate between types of DM: DM type 1 and 2, lack of insulin and insulin resistance, respectively. Yet, a lesion in the head of pancreas may result in atrophy of pancreas, endocrine pancreatic insufficiency and lack of insulin known as DM type 1. And such a lesion may lead to hard pancreas during PD with decreased PF rate (as previously described). This conclusion and discrepancies regarding DM and PF in current scientific literature should lead to reassess current definition of MS. Also, this study (showing only obesity as an independent factor of PF among MS criteria) and divergences in literature suggest that the understanding of fatty pancreas and soft pancreas are unresolved, probably incorrect. Indeed, manual palpation is subjective but enables an appropriate assessment for mild or massive pancreatic steatosis by simple inspection in surgical setting[29]. Yet, fatty pancreas is defined using pathological examination[30] and can be uneven in pancreas[31] compelling to propose another method to assess fatty pancreas as the role of pathologist in fatty pancreas is not standardized. In preoperative setting, MRI is currently considered as being as effective as histology when assessing fatty infiltration[32]. Still, a consensual and standardized histopathological examination assessing fatty infiltration[30] and fibrosis[33] of pancreatic parenchyma is required, as it has been proposed in non-alcoholic fatty liver disease (NAFLD)[34]. Also, like in NAFLD, microcirculation disorders should be investigated in fatty pancreas: in NAFLD, microcirculation has been reported as being altered[35] potentially leading to an increased mortality after hepatectomy[36]. Ischemic process related to microcirculation disorders in fatty pancreas could explain an increased rate of pancreatic fistula and pancreatic insufficiency.

Finally, results of this study should be mitigated owing to usual flaws. This series has been recorded retrospectively (in spite of a prospective inclusion). The length of the study - more than a decade - was required to reach a proper number, so management may have changed during the timeline. In the same way, different surgeons from two centres have been recorded and may have improved. Then, in-hospital mortality may be discussed due to a high rate (6%). Indeed, this rate seems to be overestimated as it is calculated as overall in-hospital mortality: in-hospital 30-d mortality and in-hospital 90-d mortality reached 4% and 6%, respectively. These results are in accordance with previous occidental studies[37], obviously, not as impressive as expert centre outcomes[38] including in France[39]. Yet, we believe that despite its retrospective design and mortality rate, this report, the first of its kind, should lead to reassess concepts of fatty pancreas and MS.

This study confirmed soft pancreas, pancreatic duct diameter < 3 mm and obesity as independent factors of PF after PD. Also, the supposed link between MS and PF after PD was not observed in the present series. Further investigations should be designed, mainly in order to confirm these results and to homogenize concepts of MS and fatty pancreas.

COMMENTS

Background

With a rising incidence in western countries and association with various digestive disorders, metabolic syndrome (MS) has become a hot topic in digestive surgery including in pancreatic resection (due to fatty pancreas).

Research frontiers

Theoretically, as MS is related to fatty pancreas and fatty pancreas is related to pancreatic fistula, pancreatic fistula occurrence should increase in patients presenting with MS and undergoing pancreaticoduodenectomy. Also, as pancreatic fistula is related to an increased postoperative mortality, postoperative mortality should be increased. Yet, no analysis of perioperative outcome after pancreaticoduodenectomy has been reported.

Innovations and breakthroughs

When this analysis showed independent factors of pancreatic fistula in accordance with previous reports, the supposed link between MS and pancreatic fistula after pancreaticoduodenectomy was not observed in the present series. Further investigations should be designed, mainly in order to

confirm these results and to homogenize concepts of MS and fatty pancreas.

Applications

MS should not be seen as a contraindication to pancreaticoduodenectomy.

Terminology

MS is defined by the association of three criteria among increased waist circumference or overweight/obesity, arterial hypertension, decreased serum HDL cholesterol, increased serum triglycerides and diabetes mellitus or increased fasting glucose.

Peer-review

This is an interest paper. It is based on important considerations and the findings are interesting.

REFERENCES

1 **Gooiker GA**, van Gijn W, Wouters MW, Post PN, van de Velde CJ, Tollenaar RA. Systematic review and meta-analysis of the volume-outcome relationship in pancreatic surgery. *Br J Surg* 2011; **98**: 485-494 [PMID: 21500187 DOI: 10.1002/bjs.7413]

2 **Hashimoto D**, Chikamoto A, Ohmuraya M, Hirota M, Baba H. Pancreaticodigestive anastomosis and the postoperative management strategies to prevent postoperative pancreatic fistula formation after pancreaticoduodenectomy. *Surg Today* 2014; **44**: 1207-1213 [PMID: 23842691 DOI: 10.1007/s00595-013-0662-x]

3 **Alberti KG**, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009; **120**: 1640-1645 [PMID: 19805654 DOI: 10.1161/CIRCULATIONAHA.109.192644]

4 **Eckel RH**, Alberti KG, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2010; **375**: 181-183 [PMID: 20109902 DOI: 10.1016/S0140-6736(09)61794-]

5 **Wu WC**, Wang CY. Association between non-alcoholic fatty pancreatic disease (NAFPD) and the metabolic syndrome: case-control retrospective study. *Cardiovasc Diabetol* 2013; **12**: 77 [PMID: 23688357 DOI: 10.1186/1475-2840-12-77]

6 **Ou HY**, Wang CY, Yang YC, Chen MF, Chang CJ. The association between nonalcoholic fatty pancreas disease and diabetes. *PLoS One* 2013; **8**: e62561 [PMID: 23671610 DOI: 10.1371/journal.pone.0062561]

7 **Gaujoux S**, Cortes A, Couvelard A, Noullet S, Clavel L, Rebours V, Lévy P, Sauvanet A, Ruszniewski P, Belghiti J. Fatty pancreas and increased body mass index are risk factors of pancreatic fistula after pancreaticoduodenectomy. *Surgery* 2010; **148**: 15-23 [PMID: 20138325 DOI: 10.1016/j.surg.2009.12.005]

8 **Shimoda M**, Katoh M, Yukihiro I, Kita J, Sawada T, Kubota K. Body mass index is a risk factor of pancreatic fistula after pancreaticoduodenectomy. *Am Surg* 2012; **78**: 190-194 [PMID: 22369828]

9 **Hwang HK**, Park JS, Park CI, Kim JK, Yoon DS. The impact of body mass index on pancreatic fistula after pancreaticoduodenectomy in Asian patients on the basis of Asia-Pacific perspective of body mass index. *JOP* 2011; **12**: 586-592 [PMID: 22072248]

10 **Tee MC**, Ubl DS, Habermann EB, Nagorney DM, Kendrick ML, Sarr MG, Truty MJ, Que FG, Reid-Lombardo K, Smoot RL, Farnell MB. Metabolic Syndrome is Associated with Increased Postoperative Morbidity and Hospital Resource Utilization in Patients Undergoing Elective Pancreatectomy. *J Gastrointest Surg* 2016; **20**: 189-198; discussion 198 [PMID: 26553267 DOI: 10.1007/s11605-015-3007-9]

11 Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser* 1995; **854**: 451-452 [PMID: 8594834]

12 **Zurlo A**, Veronese N, Giantin V, Maselli M, Zambon S, Maggi S, Musacchio E, Toffanello ED, Sartori L, Perissinotto E, Crepaldi G, Manzato E, Sergi G. High serum uric acid levels increase the risk of metabolic syndrome in elderly women: The PRO.V.A study. *Nutr Metab Cardiovasc Dis* 2016; **26**: 27-35 [PMID: 26643208 DOI: 10.1016/j.numecd.2015.10.007]

13 **Dindo D**, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205-213 [PMID: 15273542]

14 **Bassi C**, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005; **138**: 8-13 [PMID: 16003309 DOI: 10.1016/j.surg.2005.05.001]

15 **Ball CG**, Pitt HA, Kilbane ME, Dixon E, Sutherland FR, Lillemoe KD. Peri-operative blood transfusion and operative time are quality indicators for pancreatoduodenectomy. *HPB* (Oxford) 2010; **12**: 465-471 [PMID: 20815855 DOI: 10.1111/j.1477-2574.2010.00209.x]

16 **Koch M**, Garden OJ, Padbury R, Rahbari NN, Adam R, Capussotti L, Fan ST, Yokoyama Y, Crawford M, Makuuchi M, Christophi C, Banting S, Brooke-Smith M, Usatoff V, Nagino M, Maddern G, Hugh TJ, Vauthey JN, Greig P, Rees M, Nimura Y, Figueras J, DeMatteo RP, Büchler MW, Weitz J. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. *Surgery* 2011; **149**: 680-688 [PMID: 21316725 DOI: 10.1016/j.surg.2010.12.002]

17 **Veillette G**, Dominguez I, Ferrone C, Thayer SP, McGrath D, Warshaw AL, Fernández-del Castillo C. Implications and management of pancreatic fistulas following pancreaticoduodenectomy: the Massachusetts General Hospital experience. *Arch Surg* 2008; **143**: 476-481 [PMID: 18490557 DOI: 10.1001/archsurg.143.5.476]

18 **Zarzavadjian Le Bian A**, Costi R, Constantinides V, Smadja C. Metabolic disorders, non-alcoholic fatty liver disease and major liver resection: an underestimated perioperative risk. *J Gastrointest Surg* 2012; **16**: 2247-2255 [PMID: 23054903 DOI: 10.1007/s11605-012-2044-x]

19 **Mathur A**, Pitt HA, Marine M, Saxena R, Schmidt CM, Howard TJ, Nakeeb A, Zyromski NJ, Lillemoe KD. Fatty pancreas: a factor in postoperative pancreatic fistula. *Ann Surg* 2007; **246**: 1058-1064 [PMID: 18043111 DOI: 10.1097/SLA.0b013e31814a6906]

20 **Casadei R**, Ricci C, Taffurelli G, D'Ambra M, Pacilio CA, Ingaldi C, Minni F. Are there preoperative factors related to a "soft pancreas" and are they predictive of pancreatic fistulas after pancreatic resection? *Surg Today* 2015; **45**: 708-714 [PMID: 25331230 DOI: 10.1007/s00595-014-1045-7]

21 **Fu SJ**, Shen SL, Li SQ, Hu WJ, Hua YP, Kuang M, Liang LJ, Peng BG. Risk factors and outcomes of postoperative pancreatic fistula after pancreatico-duodenectomy: an audit of 532 consecutive cases. *BMC Surg* 2015; **15**: 34 [PMID: 25887526 DOI: 10.1186/s12893-015-0011-7]

22 **De Carlis LG**, Sguinzi R, Ferla F, Di Sandro S, Dorobantu BM, De Carlis R, Cusumano C, Giacomoni A, Ferrari C. Pancreatoduodenectomy: Risk Factors of Postoperative Pancreatic Fistula. *Hepatogastroenterology* 2014; **61**: 1124-1132 [PMID: 26158175]

23 **Xia X**, Huang C, Cen G, Qiu ZJ. Preoperative diabetes as a protective factor for pancreatic fistula after pancreaticoduodenectomy: a meta-analysis. *Hepatobiliary Pancreat Dis Int* 2015; **14**: 132-138 [PMID: 25865684]

24 **Bhayani NH**, Hyder O, Frederick W, Schulick RD, Wolgang CL, Hirose K, Edil B, Herman JM, Choti MA, Pawlik TM. Effect of metabolic syndrome on perioperative outcomes after liver surgery: A National Surgical Quality Improvement Program (NSQIP) analysis. *Surgery* 2012; **152**: 218-226 [PMID: 22828143 DOI: 10.1016/j.surg.2012.05.037]

25 **Cauchy F**, Zalinski S, Dokmak S, Fuks D, Farges O, Castera L, Paradis V, Belghiti J. Surgical treatment of hepatocellular carcinoma associated with the metabolic syndrome. *Br J Surg* 2013; **100**: 113-121 [PMID: 23147992 DOI: 10.1002/bjs.8963]

26 **Hall MR**, Protack CD, Assi R, Williams WT, Wong DJ, Lu D, Muhs BE, Dardik A. Metabolic syndrome is associated with type II endoleak after endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2014; **59**: 938-943 [PMID: 24360238 DOI: 10.1016/j.jvs2013.10.081]

27 **Cantiello F**, Cicione A, Autorino R, De Nunzio C, Salonia A, Briganti A, Aliberti A, Perdonà S, Tubaro A, Damiano R. Metabolic syndrome, obesity, and radical cystectomy complications: a clavien classification system-based analysis. *Clin Genitourin Cancer* 2014; **12**: 384-393 [PMID: 24713553 DOI: 10.1016/j.clgc.2014.03.001]

28 **Lin JW**, Caffrey JL, Chang MH, Lin YS. Sex, menopause, metabolic syndrome, and all-cause and cause-specific mortality--cohort analysis from the Third National Health and Nutrition Examination Survey. *J Clin Endocrinol Metab* 2010; **95**: 4258-4267 [PMID: 20534759 DOI: 10.1210/jc.2010-0332]

29 **Verma AR**, Papalois V. Evaluating steatosis in pancreatic transplant. *Exp Clin Transplant* 2011; **9**: 159-164 [PMID: 21649562]

30 **Smits MM**, van Geenen EJ. The clinical significance of pancreatic steatosis. *Nat Rev Gastroenterol Hepatol* 2011; **8**: 169-177 [PMID: 21304475 DOI: 10.1038/nrgastro.2011.4]

31 **Matsumoto S**, Mori H, Miyake H, Takaki H, Maeda T, Yamada Y, Oga M. Uneven fatty replacement of the pancreas: evaluation with CT. *Radiology* 1995; **194**: 453-458 [PMID: 7824726 DOI: 10.1148/radiology.194.2.7824726]

32 **Lingvay I**, Esser V, Legendre JL, Price AL, Wertz KM, Adams-Huet B, Zhang S, Unger RH, Szczepaniak LS. Noninvasive quantification of pancreatic fat in humans. *J Clin Endocrinol Metab* 2009; **94**: 4070-4076 [PMID: 19773401 DOI: 10.1210/jc.2009-0584]

33 **Klöppel G**, Maillet B. Pseudocysts in chronic pancreatitis: a morphological analysis of 57 resection specimens and 9 autopsy pancreata. *Pancreas* 1991; **6**: 266-274 [PMID: 1862065]

34 **Kleiner DE**, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, Ferrell LD, Liu YC, Torbenson MS, Unalp-Arida A, Yeh M, McCullough AJ, Sanyal AJ. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology* 2005; **41**: 1313-1321 [PMID: 15915461 DOI: 10.1002/hep.20701]

35 **McCuskey RS**, Ito Y, Robertson GR, McCuskey MK, Perry M, Farrell GC. Hepatic microvascular dysfunction during evolution of dietary steatohepatitis in mice. *Hepatology* 2004; **40**: 386-393 [PMID: 15368443 DOI: 10.1002/hep.20302]

36 **Zarzavadjian Le Bian A**, Costi R, Sbai-Idrissi MS, Smadja C. Liver resection and metabolic disorders: an undescribed mechanism leading to postoperative mortality. *World J Gastroenterol* 2014; **20**: 14455-14462 [PMID: 25339832 DOI: 10.3748/wjg.v20.i39.14455]

37 **Simons JP**, Shah SA, Ng SC, Whalen GF, Tseng JF. National complication rates after pancreatectomy: beyond mere mortality. *J Gastrointest Surg* 2009; **13**: 1798-1805 [PMID: 19506975 DOI: 10.1007/s11605-009-0936-1]

38 **Venkat R**, Puhan MA, Schulick RD, Cameron JL, Eckhauser FE, Choti MA, Makary MA, Pawlik TM, Ahuja N, Edil BH, Wolfgang CL. Predicting the risk of perioperative mortality in patients undergoing pancreaticoduodenectomy: a novel scoring system. *Arch Surg* 2011; **146**: 1277-1284 [PMID: 22106320 DOI: 10.1001/archsurg.2011.294]

39 **Addeo P**, Delpero JR, Paye F, Oussoultzoglou E, Fuchshuber PR, Sauvanet A, Sa Cunha A, Le Treut YP, Adham M, Mabrut JY, Chiche L, Bachellier P. Pancreatic fistula after a pancreaticoduodenectomy for ductal adenocarcinoma and its association with morbidity: a multicentre study of the French Surgical Association. *HPB* (Oxford) 2014; **16**: 46-55 [PMID: 23461663 DOI: 10.1111/hpb.12063]

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