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Prediction of Anastomotic Leakage After Pancreatic Head Resections by Dynamic Magnetic Resonance Imaging (dMRI)

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Abstract
Purpose The texture of the pancreatic tissue is a main risk factor for leakage after pancreaticojejunostomy and can be differentiated using dynamic contrast enhanced magnetic resonance imaging (dMRI). In order to identify risk factors and to assess the role of pancreatic dMRI, a cohort of patients was retrospectively reviewed.
Patients and methods One hundred seven consecutive patients were identified in the departmental database and examined by means of a standardized dMRI protocol using a 1.5-T MRI system. Signal intensity (SI) measurements (aorta, body of the pancreas, muscle tissue) were performed in the axial T1-weighted sequences before and after 25 and 60 s after i.v. application of gadolinium–diethylenetriaminepentaacetic acid. For all patients with a standardized contrast medium curve in the aorta (n=72), a muscle-normalized signal intensity curve (SIC) with SI_{ratio} was calculated. SI_{ratio}s were classified in two groups: rapid increase ($SI_{ratio} \geq 1.1$, early arterial value > portal-venous value, "soft" pancreas) and delayed increase (SI_{ratio} <1.1, "firm" or "hard" pancreas). All patients received pancreatic head resection with a duct-to-mucosa pancreaticojejunostomy. The dMRI data was correlated with prospectively acquired clinical data.
Results Leakage of the pancreaticojejunostomy occurred more frequently (12/37 vs. two of 35, 32% vs. 6%, p=0.006) in patients with a rapid increase and an $SI_{ratio} \geq 1.1$ ("soft" pancreas, n=37) compared to those with delayed perfusion (SI_{ratio} <1.1, "hard" pancreas, n=35). The more severe type B and C anastomotic leakages occurred only in the group of patients with $SI_{ratio} \geq 1.1$. Patients with a rapid increase had significantly better preoperative American Society of Anesthesiologists staging, lower carbohydrate antigen 19-9 values, and smaller tumor sizes. Most of them had not only benign tumors but also longer postoperative hospital stay, in comparison to patients with delayed perfusion (SI_{ratio} <1.1). Multivariate analysis revealed SI_{ratio} of ≥1.1 to be the only preoperative parameter predicting leakage significantly with an odds ratio of 7.9.

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Conclusion dMRI with SI_{ratio} calculation provided reliable information for the prediction of pancreatic texture. Patients with a $SI_{ratio} \geq 1.1$ had a 7.9-fold increased risk of anastomotic leakage and a prolonged hospital stay. SIC with measurements of SI_{ratio} in dMRI could therefore define patients at risk for anastomotic leakage.

Keywords Pancreatic surgery · Anastomotic leakage · Dynamic magnetic resonance imaging

Introduction

The mortality of pancreatic head resection, with or without pylorus preservation, has significantly declined over the past decades and lies below 5% in experienced centers.[1,2] The morbidity of this procedure is, however, high with 30[1–3] to 60%.[4,5] The pancreatic anastomosis is the "Achilles' heel" in pancreatic surgery.[6,7] Leakage of the pancreaticointestinal anastomosis is the main trigger for other morbidities after this procedure. Clinically, a leakage may present as a pancreatic–cutaneous fistula, intraabdominal abscess, delayed gastric emptying, intestinal atony, or it can result in sepsis and hemorrhage leading to a significant mortality.[1,7,8] The two common reasons for leakage of pancreatic anastomosis are a "soft" pancreatic texture and a small pancreatic duct size.[9–12] Chronic pancreatitis leads to fibrotic, "hard" pancreatic tissue. Anastomotic leakage is therefore observed less frequently after resections due to chronic pancreatitis, compared with resections due to cancer.[13] The reported incidence of leakage lies between 0 and 30% and may represent a marked underestimation due to selection bias as well as publication bias.[7] Since duct size is an objective parameter the surgeon can easily identify an anastomosis being at risk for leakage during the operation and can spontaneously change the operation procedure; for instance one can decide to switch to another anastomosis technique.

The degree of "softness" of the pancreatic tissue and its role in estimation of an anastomosis being at risk remains to be a problem. Reliable preoperative diagnostic tools or risk scores for prediction of a soft texture are currently not available. The normal exocrine fluid output of the "soft" pancreatic tissue, as compared to that of the fibrotic ("hard") tissue in patients with chronic pancreatitis, has been described as another risk factor for leakage.[7,14] It is therefore not proven that "soft" correlates with "normal" healthy pancreatic tissue. In magnetic resonance imaging (MRI), Sittek and his coauthors could observe various patterns of pancreatic perfusion depending on various pancreatic textures.[15]

The aim of this study was to evaluate the role of dynamic magnetic resonance imaging (dMRI) in prediction of soft pancreatic texture and leakage of the pancreatic anastomosis. Additionally, it was attempted to identify other risk factors for leakage of the pancreatic anastomosis.

Materials and Methods

Between 2002 and 2007, a total of 217 patients underwent a pancreatic resection (Kausch–Whipple resection or pylorus-preserving pancreaticoduodenectomy) due to a pancreatic head tumor in the Department of Surgery. All patients were identified in the prospective departmental pancreatic database.[1,16–18] During this 5-year period, a total number of 107 consecutive patients with a sonographically suspected tumor of the pancreas head were evaluated by dMRI prior to resection. All patients with a dMRI in our institution were included in the present analysis. The data of the latter patients examined comprised demographics; pathology report; tumor, node, metastasis stage; and International Union Against Cancer classification, preoperative presenting symptoms, preoperative procedures (e.g., biliary stent), lab work (including tumor marker carbohydrate antigen (CA) 19-9), the American Society of Anesthesiologists (ASA) score, details of the surgical therapy (including blood loss and blood transfusions), the hospital course (including complications), and the postoperative survival.

Follow-up was performed through personal contact with the patient or patient's primary physician and was terminated on June 1 2008 or at patient's death. All deaths occurring within 30 days after surgery or throughout the hospital stay were classified as surgical mortality. In all patients, drains were placed at the pancreaticojejunostomy and at the hepaticojejunostomy site.

An anastomotic leakage was defined according to the International Study Group on Pancreatic Fistula (ISGPF) definition.[19] A grade A leakage is a so-called "biochemical, transient fistula" and has no clinical impact. A grade A leakage requires little change in management or deviation from the normal clinical pathway. A grade B leakage requires a change in the patient management or an adjustment in the clinical pathway. It usually leads to a delay in discharge, to readmission, or to discharge of the patient with drains in situ. A grade C leakage leads to a major change in the clinical management or a deviation from the normal clinical pathway. A deteriorating clinical status with a grade C leakage together with sepsis and an organ dysfunction may require reexploration in an attempt to repair the site of leakage with wide peripancreatic drainage, or a conversion to alternative pancreaticoenteric anastomosis, or a complete pancreatectomy.

Surgical Technique of Pancreatic Anastomosis

Within 1 to 10 days (median 3 days) after the dMRI, all patients underwent a pancreatic head resection (Kausch–

Whipple or pylorus-preserving procedure) with reconstruction as duct-to-mucosa pancreaticojejunostomy. The two-layer pancreatointestinal anastomosis was standardized as follows: After mobilization of the pancreatic remnant, the inner suture layer was placed on the pancreatic duct. Usually eight stitches were required (resorbable monofilament 5-0 sutures), the posterior wall was sutured from inside to outside, the anterior wall from outside to inside. The mesenteric surface of jejunum was approximated to the pancreas stump. The posterior wall of the outer suture layer was sewn in a running manner after placing a knot on the cranial edge of the pancreas (resorbable monofilament 4-0 sutures). A small incision corresponding to the localization and diameter of the pancreatic duct was made on the antimesenteric surface of the jejunum and the inner layer (duct to mucosa) was completed by stitching the previously placed sutures and tying them gently. The anastomosis was completed by a running suture of the outer anterior wall with the previously placed suture (serosal surface of the pancreatic remnant to seromuscular layer of jejunum; Fig. 1). Two soft drains were placed in every patient: one at the pancreatic anastomosis and one close to the hepaticojejunostomy.

Dynamic MRI

All patients underwent a MRI examination of the pancreas using the same 1.5-T system (Magnetom Vision, Siemens Medical Solutions, Erlangen, Germany). The sequence protocol is described in Table 1 in detail. All patients underwent standard sequences for the description of the morphology followed by a native T1-weighted fat saturated sequence centered on the body of the pancreas with a slice thickness of 5 mm without a gap. The sequence was repeated after intravenous administration of 0.1 mmol/kg bodyweight gadolinium–diethylenetriaminepentaacetic acid (Gd-DTPA; Magnevist®, Bayer Schering, Berlin, Germany) via an automatized injection with a flow rate of 2 ml/s using a 21-G i.v. line in a cubital vein, followed by a saline flush with 40 ml isotonic saline solution. The T1-weighted fat saturated sequence was repeated approximately 25 and 60 s after application of contrast medium in the axial plane, after 2 min in a coronal plane, and after 2.5 min for the termination of the examination in an axial plane without fat saturation. In order to compare pancreas-healthy individuals with the resected patients, the MRI data of 15 age- and gender-correlated patients without an apparent pancreatic or liver disease were evaluated within 12 months after the dMRI examination following the above mentioned protocol.

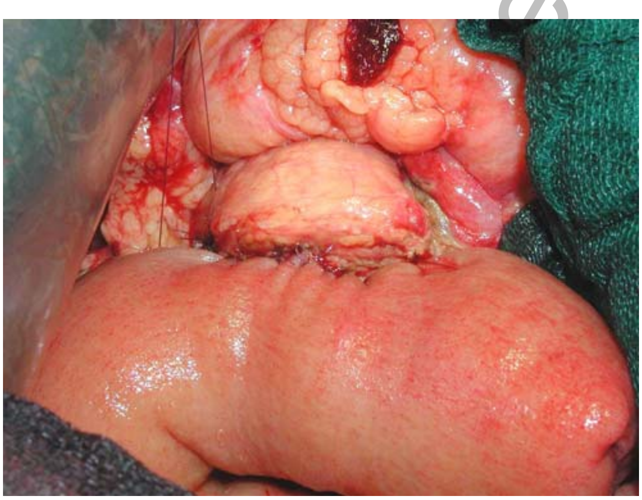

Figure 1 Duct-to-mucosa pancreaticojejunostomy: the posterior wall of the outer suture row is completed as the complete duct-to-mucosa suture. The anterior portion of the outer suture row between pancreas capsule and seromuscularis of the jejunum is still missing.

dMRI Image Evaluation

A measurement of the signal intensity (SI) was carried out in different regions of interests (RoIs) with at least 16 pixels for reliable results. The first RoI was measured in the pancreatic tissue at the estimated resection line, with and without the pancreatic duct. Further, RoIs were inside the aorta at the axial plane of the pancreas body and inside the paravertebral muscle (spinal erector muscle) for the normalization of the measurements (Fig. 2a–d). In the initial evaluation, all patients with a nondiagnostic contrast media application (all patients with an increase of the SI in the aorta after the initial arterial peak) were excluded. The measurement results in the pancreas were normalized by setting the increase in the pancreas in relation to the increase in the muscle according to the formulas described in Table 2.

The patients were classified into two groups according the pattern of perfusion following the ratio: $SI_{ratio} = \left(\frac{SI_{ea}}{SI_{pv}}\right)$. SI_{ea} was defined as the signal intensity in the early arterial phase and SI_{pv} as the portal-venous phase after the application of contrast. If the pancreatic tissue demonstrated a muscle-normalized SI_{ratio} of ≥1.1, the patients were assigned to group 1 (normal perfusion of the organ). Patients who demonstrated an SI_{ratio} <1.1 were assigned to group 2 (decreased perfusion of the organ). An age-matched group of 15 volunteers without history of a pancreatic disease were evaluated using the same examination and evaluation protocol.

Statistical Analyses

The primary endpoint of the study was the leakage of the pancreatic anastomosis. A Fisher's exact test was performed comparing the two groups. A chi-square test was performed comparing various patient data and the perfusion values. A multivariate analysis (logistic re-

Table 1 Examination Protocol for the MRI of the Pancreas

	T1 ax	T2 TSE ax	T1 fs ax	MRCP (HASTE)	MRCP (RARE)	T1 fs ax	T1 fs cor	T1 ax
TR/TE	121/4.1	5,000/120	132.4/2.3	4.4/64	2,800/1,100	132.4/2.3	132.4/2.3	121/4.1
Matrix	256×256	256×256	256×256	256×256	256×256	256×256	256×256	256×256
FoV (mm)	300×300	300×300	300×300	300×500	300×400	300×300	500×300	300×300
Slice thickness (mm)/gap	5/5	5/5	5/0 (pancreas)	6/0	50/na	5/0 (pancreas)	5/5	5/5
TA (s)	16	17	16	16	6	16	17	16
Contrast (time after i.v. administration)	–	–	–	–	–	+ (25 and 70 s)	140 s post	Yes

ax axial, *MRCP* magnetic resonance cholangiopancreaticography, *HASTE* half-Fourier acquisition turbo spin echo sequence, *RARE* rapid acquisition with relaxation enhancement, *fs* spectral fat saturation, *cor* coronal, *TR* time of repetition, *TE* echo time, *FoV* field of view, *TA* time of acquisition, *na* not applicable

gression) was calculated with an odds ratio (OR) for all parameters described. Predicting factors for the leakage were examined by univariate and multivariate analyses, using Cox's proportional hazards including a calculation of the odds ratio for all parameters described. Significance was accepted at the probability level of 0.05. All statistical calculations were performed using the SAS software (release 9.01; SAS Institute Inc., Cary, NC, USA).

Results

All examinations were performed with the same sequence protocol without any study violation. A total of 107 patients (median age 67.5 years, range 30–89 years, 65 men, 42 women) were included in the evaluation. In 72 patients (median age 67 years, range 30–89 years, 42 men, 30 women), the early arterial SI in the aorta was higher than the portal venous SI, showing the correct timing of the

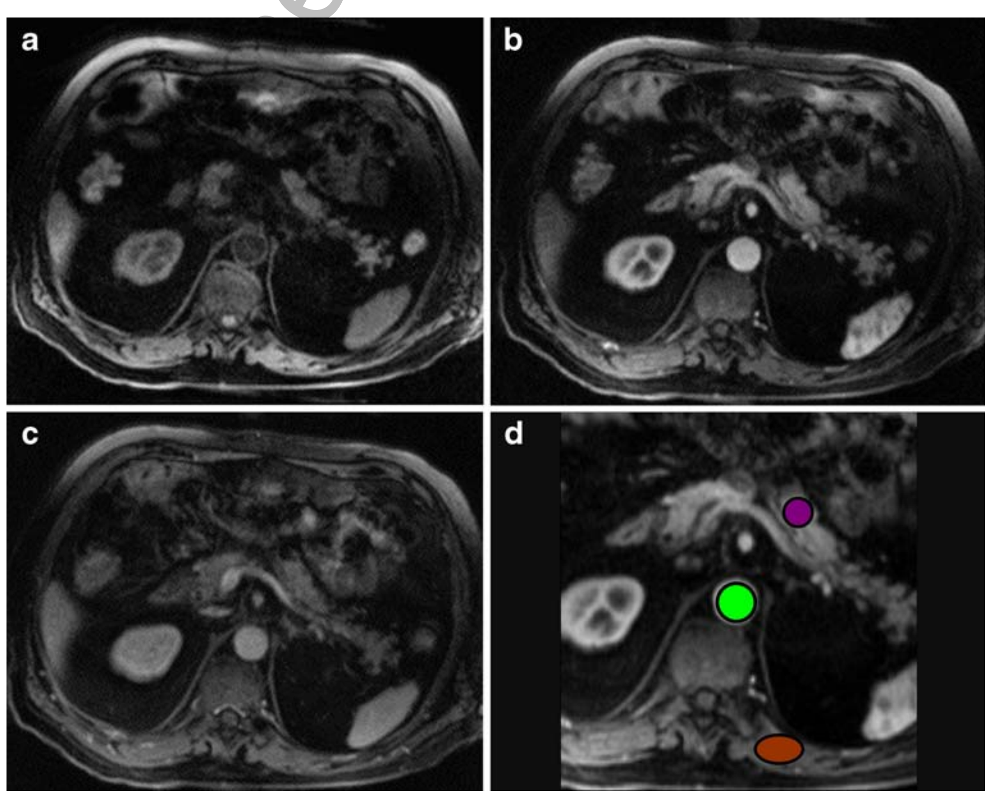

Figure 2 a–**d** T1-weighted images of the pancreas with fat saturation, demonstrating the contrast enhancement in the body of the pancreas. **a** Native, **b** 25 s, and **c** 60 s after b.w. adapted i.v. administration of Gd-DTPA (Magnevist®). **d** Illustrates the localization of the regions of interest for the measurement of the signal intensities. The *colors* indicate the different tissues: *purple* = pancreatic parenchyma at the localization of the presumed resection margin, *green* = abdominal aorta at the height of the pancreas, and *brown* = muscle tissue of the paravertebral spine muscle.

Table 2 Formulae for the Evaluation of the Signal Intensity Measurements

Native: $SI_{native} = \left\{ \left[\frac{SI(pancreas_{nativ})}{SI(muscle_{nativ})} \right] - \left[\frac{SI(pancreas_{nativ})}{SI(muscle_{nativ})} \right] \right\} \times 100\%$

"Nativ" in der Formel muss noch durch "native" ersetzt warden

Early arterial: $SI_{ea} = \left\{ \left[\frac{SI(pancreas_{ea})}{SI(muscle_{ea})} \right] - \left[\frac{SI(pancreas_{nativ})}{SI(muscle_{\ nativ})} \right] \right\} \times 100\%$

Portal venous: $SI_{pv} = \left\{ \left[\frac{SI(pancreas_{pv})}{SI(muscle_{pv})} \right] - \left[\frac{SI(pancreas_{nativ})}{SI(muscle_{nativ})} \right] \right\} \times 100\%$

contrast media application. These 72 patients fulfilled criteria for the further examination (Table 3).

Perioperative Course

An uncomplicated postoperative course was observed in 31% of all patients (22/72). The overall morbidity rate was 69% (50/72); the postoperative mortality was 1.4% (one of 72). A classic Kausch–Whipple resection was performed in 27 patients (37.5%), a preservation of the pylorus-preserving pancreatoduodenectomy (PPPD) could be achieved in 45 patients (62.5%). Leakage of the pancreaticojejunostomy was observed in 14 patients (19.4%): grade A leakage in nine patients, grade B leakage in three, and grade C leakage requiring relaparotomy in two patients. In one of the latter patients, the anastomosis was converted; in the other patient, a complete pancreatectomy was necessary. This patient died subsequently on the 24th postoperative day. A leakage of the hepaticojejunostomy occurred in four patients (5.5%; Table 4). Seven (9.7%) patients required relaparotomy for complications, postoperative bleeding occurred in three (4.2%) patients, nine (12.5%) patients developed a delayed gastric emptying, and five (6.9%) patients presented with an intraabdominal abscess (Table 4).

Table 3 Correlation of Demographic, Histological, and Preoperative Parameters with SI_{ratio}

	$SI_{ratio} \geq 1.1$ (n=37)	$SI_{ratio} < 1.1$ (n=35)	p value
Age (years)	67 (30–89)	68 (40–85)	0.65
Gender (men vs. women)	21 vs. 16	21 vs. 14	0.76
ASA score (I/II vs. III/IV)	28 vs. 9	17 vs. 18	0.004
Diabetes preoperative	9	14	0.22
Bilirubin preoperative (g/dl)	1.5 (±10.7)	3.5 (±15.9)	0.48
CA 19.9 preoperative (U/l)	22 (±1.233)	152 (±2.724)	0.01
Albumin preoperative (g/dl)	33 (±5)	34 (±4)	0.79
Malignancy	30	27	0.64
Chronic pancreatitis	3	6	0.23
Benign tumor	7	2	0.05
Size of tumor (mm)	23 (±14)	32 (±16)	0.007

Table 4 Correlation of Procedural and Postoperative Parameters with SI_{ratio}

	$SI_{ratio} \geq 1.1$ (n=37)	$SI_{ratio} < 1.1$ (n=35)	p value
Procedure (Whipple vs. PPPD)	7 vs. 30	9 vs. 26	0.09
Complications (all)	29	20	0.07
Leakage pancreaticojejunostomy[a]	12	2	0.006
ISGPS leakage grade A[a]	7	2	
ISGPS leakage grade B[a]	3	0	
ISGPS leakage grade C[a]	2	0	
Leakage of the hepaticojejunostomy	3	1	0.35
Intraabdominal abscess	3	2	1
Blood loss (ml)	800 (±483)	750 (±587)	0.27
Operation time (min)	360 (±74)	351 (±113)	0.97
Mortality	2 (of 107)	0	0.49
Hospital stay (days)	20 (12–167)	17 (9–60)	0.05

[a] According to ISGPS definition of leakage[19]

Histopathology revealed cancer in 54 patients (75%): 33 ductal adenocarcinoma, five distal bile duct carcinoma, five carcinoma of Vater's papilla, 11 miscellaneous malignant tumors. Nine (12.5%) patients were diagnosed with a chronic pancreatitis, and nine (12.5%) patients had a benign lesion (for example noninvasive intraductal papillary mucinous neoplasm).

Evaluation of dMRI and Correlation with Clinical Parameters

Thirty-seven of the 72 patients who qualified for the final analysis (median age 67 years, range 30–89 years, 21 men, 16 women) revealed a pancreatic perfusion with an $SI_{ratio} \geq 1.1$. Thirty-five patients (median age 68 years, range 40–85 years, 21 men, 14 women) had an $SI_{ratio} < 1.1$. All pancreas-healthy patients in the control group showed an $SI_{ratio} \geq 1.1$. An $SI_{ratio} \geq 1.1$ was therefore equivalent to a "normal" pancreatic perfusion.

A comparison of the perfusion in dMRI and the clinical parameters revealed the following statistically significant results. In comparison to patients with a delayed perfusion ($SI_{ratio} < 1.1$), those with a "normal" perfusion ($SI_{ratio} \geq 1.1$) were significantly more often classified as ASA group I/II (no or mild comorbidities, p=0.004). These patients had lower preoperative CA 19-9 levels (22 vs. 152 U/l, p=0.01) and a smaller tumor size (23 vs. 32 mm, p=0.007).

Regarding the postoperative results, patients with a normal perfusion ($SI_{ratio} \geq 1.1$) had statistically significant higher rate of leakage of the pancreaticojejunostomy (p=0.006); 12 of 14 leakages (86%) occurred in patients with a normal perfusion ($SI_{ratio} \geq 1.1$) compared to only two of 14 leakages in patients with a delayed ($SI_{ratio} < 1.1$) perfusion. All grade B and C leakages occurred in patients with a normal perfusion. Two of 12 patients required relaparotomy (grade C) and three patients were discharged with drains in place, or needed a reintervention (grade B). In contrast to these findings, only in two patients with an signal intensity curve (SIC) <1.1 that a “biochemical” leakage (grade A) occurred. Patients with a normal perfusion had a significantly longer hospital stay (20 vs. 17 postoperative days, $p=0.05$) and were more likely to have other postoperative complications, resulting in an overall morbidity rate of 78% (29/37 vs. 21/35). This difference, however, was of no statistical significance ($p=0.07$; Table 4).

In order to reveal predictive factors of an anastomotic leakage, all preoperative parameters were evaluated in a multivariate analysis. The $SI_{ratio}\geq1.1$ was shown to be the only parameter with a strong statistically significant correlation with the postoperative leakage ($p=0.0042$, odds ratio (OR) 7.92). All other parameters, such as ASA score, chronic pancreatitis, pancreatic cancer, tumor size, diabetes, etc., revealed no significant correlation (Table 3). The perfusion pattern in dMRI was therefore the only preoperative parameter predicting the probability of having a postoperative leakage (OR 7.92). The risk of developing a leakage was 7.9-folds higher in patients with a normal pancreatic perfusion and an $SI_{ratio}\geq1.1$ in dMRI, in comparison to those with an SI_{ratio} <1.1 in dMRI (Table 5).

Discussion

One of the challenges following a pancreaticointestinal reconstruction is the prevention of an anastomotic leakage. A leakage is a critical factor influencing postoperative morbidity and mortality.[7,20,21] As a result, over 70 different techniques for reconstruction of the pancreatic remnant following pancreatic head resection have been described.[7] The multitude of the suggested modifications, however, reflects that none of the techniques is perfect enough to convince every pancreatic surgeon for every intraoperative situation (“soft” or “firm” gland). Furthermore, there are no objective criteria to assess the texture of the pancreas prior to the operation, in order to adapt the surgical technique adequately and to inform the patients at risk for anastomotic leakage. The texture of the pancreatic tissue is explained by its pathophysiology. The natural texture is “soft” with a main pancreatic duct of a maximum diameter of 3 mm. The perfusion of this type of gland is not impaired. Following a chronic pancreatitis, the gland is usually fibrotic and firm with an impaired perfusion.[14] Other pancreatic disorders such as solid or cystic pancreatic tumors can lead to a variety of texture changes from “soft” to firm” along with different perfusion pattern.[22–24] Various pancreatic perfusion behavior in dMRI correlates with changes of the pancreatic texture.[15] Pancreatic perfusion in dMRI, calculated as SIC by measuring the SI_{ratio} was therefore studied as a predictor for an anastomotic failure. It was examined as a possible objective measure for the assessment of the texture of the pancreatic remnant.

Table 5 Multivariate Analysis (Logistic Regression) of Preoperative Parameters Correlated with Leakage of the Pancreaticojejunostomy

Parameter	p value
$SI_{ratio}\geq1.1$	0.0042 (OR 7.92)
Diabetes	0.75
Malignancy	0.29
Chronic pancreatitis	0.14
Size of tumor (mm)	0.65
ASA I+II vs. III/IV	0.09
Albumin preoperative (g/dl)	0.21
CA 19.9 preoperative (U/l)	0.47

dMRI Pancreatic Imaging

The main protocol in 1.5-T MRI consists of a standard evaluation with T2-weighted (turbo-) spin echo sequences and diffusion-weighted images of the upper abdomen, with a calculation of the resulting apparent diffusion coefficients. The magnetic resonance cholangiopancreaticography is performed by fast T2-weighted images in half-Fourier acquired T2-weighted single-shot turbo spin-echo sequences technique and rapid acquisition with relaxation enhancement technique. The native protocol is completed by T1-weighted images, with and without fat saturation for the delineation of the pancreas tissue. These sequences are followed by application of an MR contrast media, usually Gd-DTPA, in order to describe the contrast kinetics of tumors in terms of them being hypo-, iso-, or hyperintense after contrast media application. The examination is terminated by repeating the T1-weighted sequences in axial and coronal planes.[25] The examination can be performed with an axial thin-sliced T1-weighted sequence with fat saturation in order to visualize the pancreas in the early arterial, as well as in the portal-venous phase with excellent delineation of the tissue. The limitations, however, are in the exact description of vessel involvement, in case of an abnormal localization of the pancreas tissue, or of the upper abdominal vessels.[25–28] Another examination mode is the use of a coronal three-dimensional (3D) sequences as an angiographic examination, usually as a 3D volume interpolated breath-hold examination sequence. The advantage of this sequence is the high resolution with a voxel size of 1 mm^3. The disadvantage, however, is the sequence inherent signal-to-noise ratio, leading to a decrease in the quality of the evaluation of the pancreatic tissue. The results of the described techniques are, nevertheless, encouraging, and both methods are used in the imaging technique of the pancreas.[25,26] The protocol used in this study consisted of the described thin slice axial T1-weighted sequence with the advantage of integrating delineation of morphology and the dynamic contrast enhancement aspect.

Exact imaging is essential for the exact differentiation of the tumor, the vessel infiltration of the arterial and venous vessels, and for staging of possible metastases.[25,29,30] Only a small number of previous investigators, however, have assessed pancreatic perfusion by performing a semiquantitative analysis of gadolinium enhancement parameters.[31–33] The quantitative analysis of regional blood perfusion using dMRI has been described for different tissues.[31–33] Although the study of Bali et al.[34] proposed an approach to quantify parameters with a so-called “one compartment model” for the pancreatic parenchyma, there is currently no standard of reference available for the perfusion parameters of the pancreas. Using semiquantitative methods, Coenegrachts and coworkers described a statistically significant difference between patients with chronic pancreatitis and healthy volunteers in the so-called “wash in time” as well as in the “time to inflow deceleration”. They demonstrated a better contrast media enhancement in healthy volunteers in all parts of the pancreas.[31] Other studies from Tajima and his coworkers[32,33] applied the so-called “time intensity curves”. This parameter was calculated as a function of signal intensity (SI post−SI pre)/SI pre×100%) and lead to a differentiation between two various tissue types: those with a good perfusion (rapid rise to a peak in the early arterial phase followed by a rapid decline) and those with a restricted perfusion (slow rise to a peak beginning at the portal-venous phase followed by a slow decline or very slow rise to a late peak followed by a decline or a plateau). These groups could be differentiated using different contrast media behavior 25 and 60 s after contrast media application. Similar to the present study the study of Tajima and his coworkers was aimed to predict possible anastomotic leakage. Their study, however, had major limitations concerning the reliability. The authors did not mention the measurement of the pancreatic duct, which was obviously inside the RoI. This leads to false measurements, since the content of the duct, which is water like, shows no contrast media enhancement, resulting in reduced signal intensity. Furthermore, the authors did not consider the different normalization levels of the images, or the different circulation times of the patients. These issues alter the signal intensity curves as well. As a significant modification, the present study included only patients who had an increase of the signal intensity in the aorta in the first arterial phase and revealed a decrease of the values in the second measurement. In the current study, only the tissue and not the duct was measured. This led to RoI which included only 6 to 8 pixels in some patients. The measurement was therefore more reliable than measuring the duct. Furthermore, the signal intensities were normalized in every patient with a very slow enhancing muscle tissue, in order to obtain more intra- as well as interindividually comparable measurements. The image-inherent noise level was also taken into consideration.[35]

Prediction of Anastomotic Leakage

In this series of 72 pancreatic head resections, 14 patients (19.4%) developed a leakage (nine grade A, three grade B, two grade C) postoperatively. This was a reasonable value compared to 1,507 patients of a multicenter database having a leakage rate of 26.7% according to the ISGPF definition.[9] In this study, the less severe type of leakage (grade A) occurred more frequently (64% vs. 48%). As a main result, it could be demonstrated that patients with a normal perfusion ($SI_{ratio} \geq 1.1$) had significantly higher rate of leakage ($p=0.006$) and a higher rate of more severe leakage types. All grade B and C leakages occurred in patients with $SI_{ratio} \geq 1.1$. Consecutively, patients with a normal perfusion ($SI_{ratio} \geq 1.1$) had a significantly longer hospital stay ($p=0.05$) and were more likely to have other postoperative complications ($p=0.07$). In a multivariate analysis, it could be shown that the $SI_{ratio} \geq 1.1$ was the only parameter revealing a strong statistically significant correlation with postoperative leakage ($p=0.0042$) with an odds ratio of 7.92. This implies that the risk of anastomotic failure in patients with a normal pancreatic perfusion is 7.92-folds higher than those with an impaired perfusion. The cutoff value for the SI ratio was chosen as a consequence of, and an improvement to the studies by Tajima,[32,33] who did not include the normalization of the values according to the muscle tissue.

Type of Resection

A recent meta-analysis[36] demonstrated no differences between the types of anastomosis (pancreatojejunostomy or pancreatogastrostomy) regarding gastric emptying time, pancreatic exocrine or endocrine insufficiency, or findings of ulcerative disorders in the endoscopy. The rate of pancreatic remnant related relaparotomies was, however, higher in the group of the patients who underwent pancreatojejunostomy.[37,38] Although in the present study pancreaticojejunostomy using a duct-to-mucosa technique was performed in all cases, there was a rate of 14/72 anastomotic leakages. Other groups such as Hayashibe and coauthors[39] described a series of 55 consecutive patients without a pancreatic anastomotic leakage after duct-to-mucosa anastomosis in all cases. The cited group considered this kind of anastomosis to be safe, having low complication rates, being reliable and favorable for the anastomosis after pancreatoduodenectomy. The findings of this study are in accordance with the leakage rate described in the literature,[40–42] which lies between 5% and 25% in patients after pancreaticojejunostomy.

Prediction of a Soft Pancreas

As a main result, a strong correlation was found between an $SI_{ratio} \geq 1.1$ and a pancreas parenchyma of age-correlated healthy volunteers showing the same contrast enhancement. A similar finding has been described by Tajima et al.,[32] who described the perfusion of the pancreas to be the only independent variable for the prediction of leakage. As mentioned above, this was, however, performed with a technique which was less elaborate and reliable than the one in the present study. Patients with pancreas tumors addressed to have a resection of the pancreatic head can be categorized into two groups: (1) patients with a soft, fragile pancreas, and/or small pancreatic duct and (2) those with a fibrotic, firm pancreas, and/or dilated pancreatic duct. The first group is described to have a high risk for postoperative pancreatic anastomotic leakage, the second group to have a lower risk.[23,43,44] In the present study, there were better preoperative conditions described, along with an "objective" classification such as ASA classification, in the group with a better perfusion, which revealed a higher rate of anastomotic failure. This could lead to the assumption that objectively healthier patient are at a higher risk for anastomotic complications, due to a well-perfused soft gland. There is therefore a necessity for having other therapeutic options for patients at risk for a leakage. The change of the anastomotic technique in these patients (for instance from pancreaticojejunostomy to pancreatogastrostomy) could be a possible option (Fig. 3).

In summary, the present study demonstrated in particular a high rate of anastomotic leakage in patients with a regular perfusion of the pancreas parenchyma. This was contradictory to the fact that these patients had a lower surgical risk in general. Using a simple method of relative perfusion quantification, based on the contrast media enhancement of

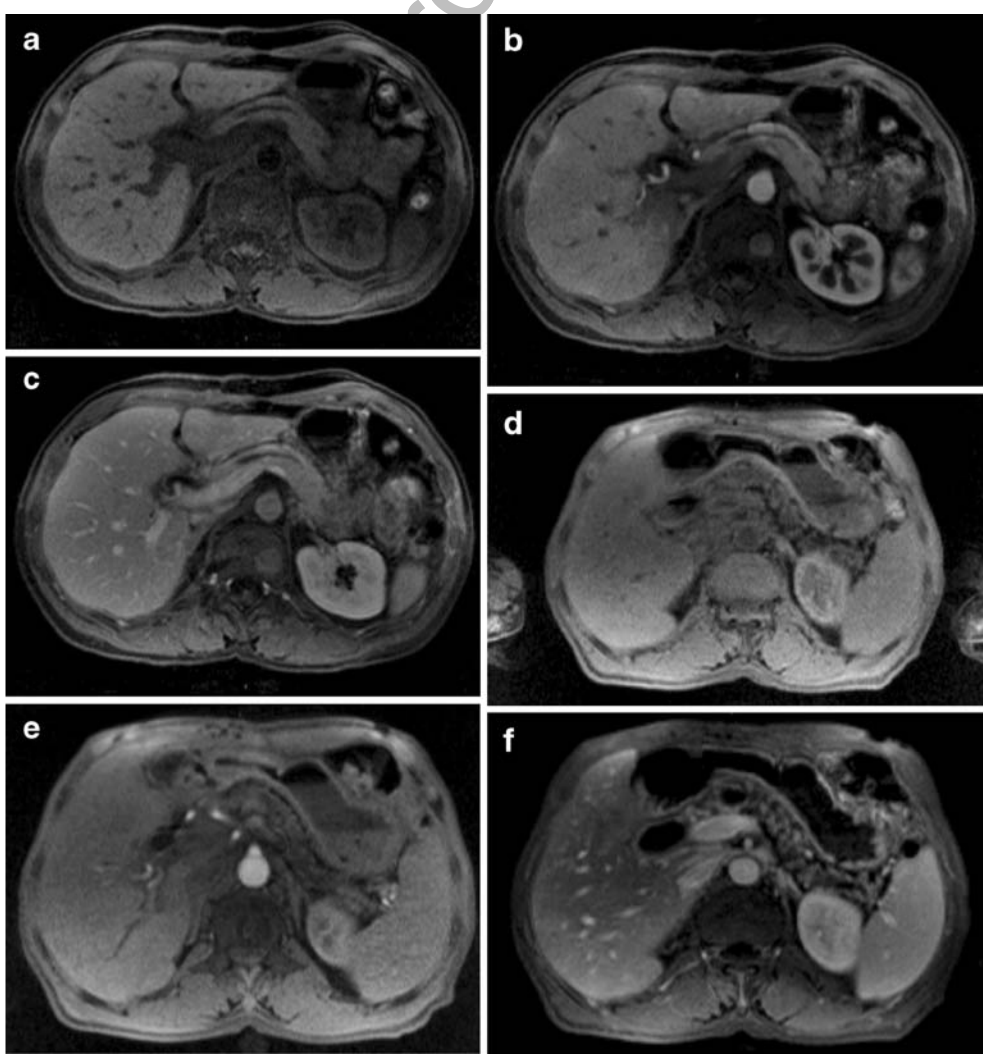

Figure 3 **a**–**f** T1-weighted images of the pancreas in a patient with a rapid increase of the SIC and a SI_{ratio} of ≥1.1 ("soft pancreas"; **a**–**c**) and in a patient with a delayed increase of the SIC and a SI_{ratio} of <1.1 ("firm pancreas"; **d**–**f**). Images **a** and **d** are native images, **b** and **e** demonstrate the early arterial phase, and **c** and **f** show the portal-venous phase.

the pancreas in relation to the aorta and the muscle tissue, it is possible to identify patients at risk for postoperative anastomotic leakage. Through applying the described dMRI technique, pancreatic surgeons can therefore preoperatively inform patients about their risk and possibly stratify these patients for other anastomotic techniques in the future.

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