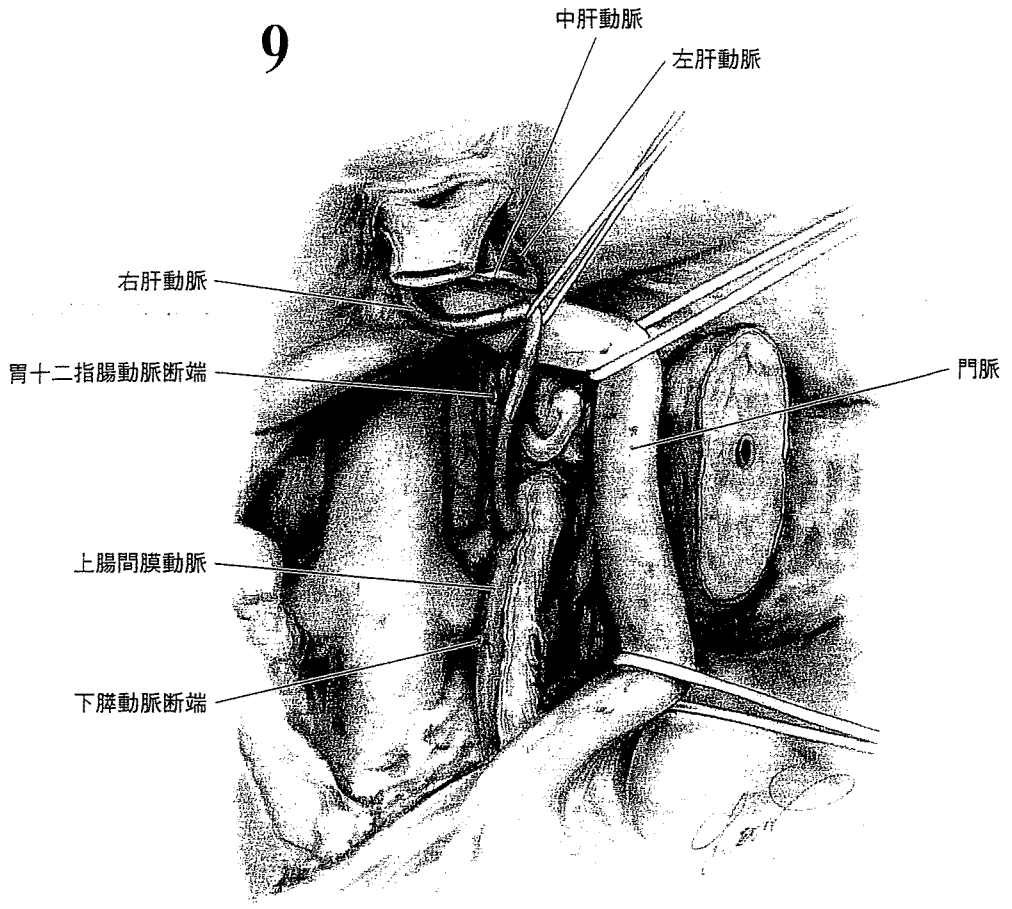


図9　標本摘出後
中，左肝動脈から総肝動脈，胃十二指腸動脈切離断端，門脈が剝離されている。門脈を左方へ牽引すると，腹腔動脈の根部および上腸間膜動脈の右半周の神経叢が郭清され外膜が根部から約4cmにわたり露出されている。この症例の右肝動脈は上腸間膜動脈の根部から約1.5cm末梢側から分枝していた

全長性に視野に現れるので，SMAの0時の部位で神経叢を切開し，右半分の神経叢切離を行うと標本摘出となる（図9）。この際，すべての切離断端組織を永久病理検査に提出する。

8. 再建術（PD-Ⅱ-A1）；膵管空腸吻合（柿田法変法[4]）

当科での再建方法は膵，胆管，胃の順に吻合するⅡ型，膵空腸吻合を柿田法変法で行っている（PD-Ⅱ-A1）。再建の前に，腹腔内を生理食塩液3lで，洗浄を行うとともに止血を確認する。再建空腸を結腸間膜に通して膵切離部に誘導する。空腸切離部から約5cmの部位で膵管径の1/2～2/3長の切開を入れる。図10a，bで示すように，膵を貫通し，空腸の漿膜筋層との間の密着吻合を4-0 Prolene糸で3～4針，膵管粘膜吻合を5-0 PDS糸で8針縫合する。膵実質の損傷を防ぐために膵実質を把持せず，膵管や空腸吻合口の視野確保に有用なinternal thoracic artery（ITA）holder[5]を使用している。2006年以降，膵管外瘻術は行っていない。

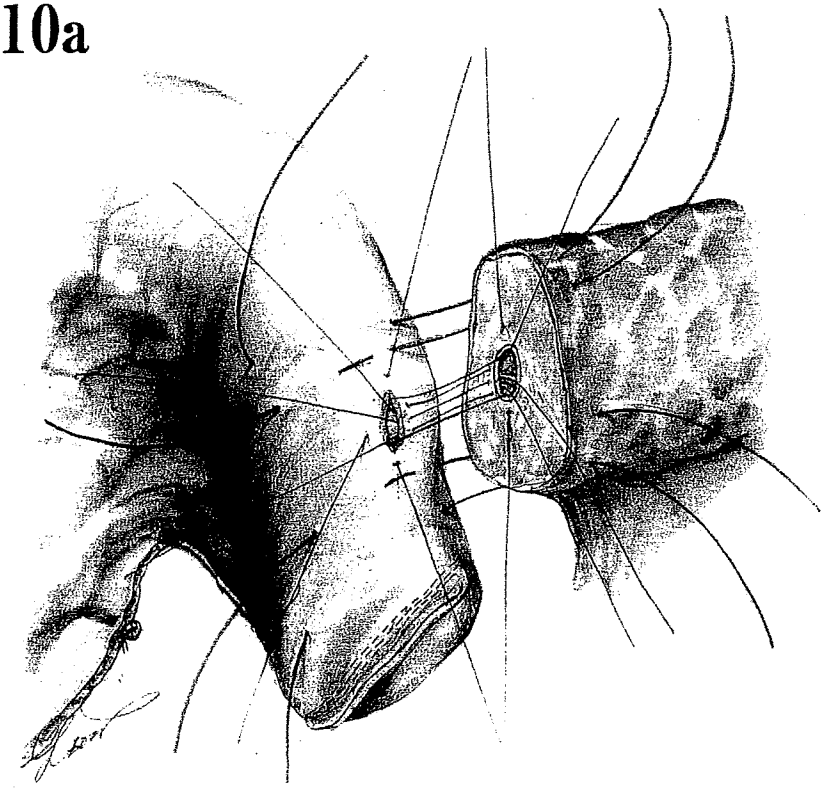
9. 肝管空腸吻合

4-0 PDS両端針を用いた連続縫合を行い，原則として胆管外瘻術は行っていない。膵空腸吻合部から，緊張のかからない部位を選び，胆管径の1/2～2/3長の切開を空腸に入れる。まず，空腸の2時方向に4-0 PDS両端針で外内方向に運針し，さらに空腸孔4時方向に内外で運針した後，結紮を行う。次に片方の針を把持し，結紮部とほぼ同部位の胆管側に針をかけ，空腸側と進み後壁の縫合を行う（図11a）。後壁が終わり，少し前壁にかかる部分でいったん針を置き，次にもう片方の針で前壁の縫合に移る。空腸側から開始し，最初の2針ほどは，胆管をかける際にかならず逆針で把持し，胆管に運針する（図11b）。前壁の運針を終えたとき先述の後壁の針と一緒に結紮する。

10. 胃空腸吻合とBraun吻合

Braun吻合は自動縫合器で行い，胃空腸吻合は，Albert-Lembert吻合で，漿膜筋層を4-0吸収糸で，全層吻合を3-0 PDS糸による連続縫合としている。

10a



10b

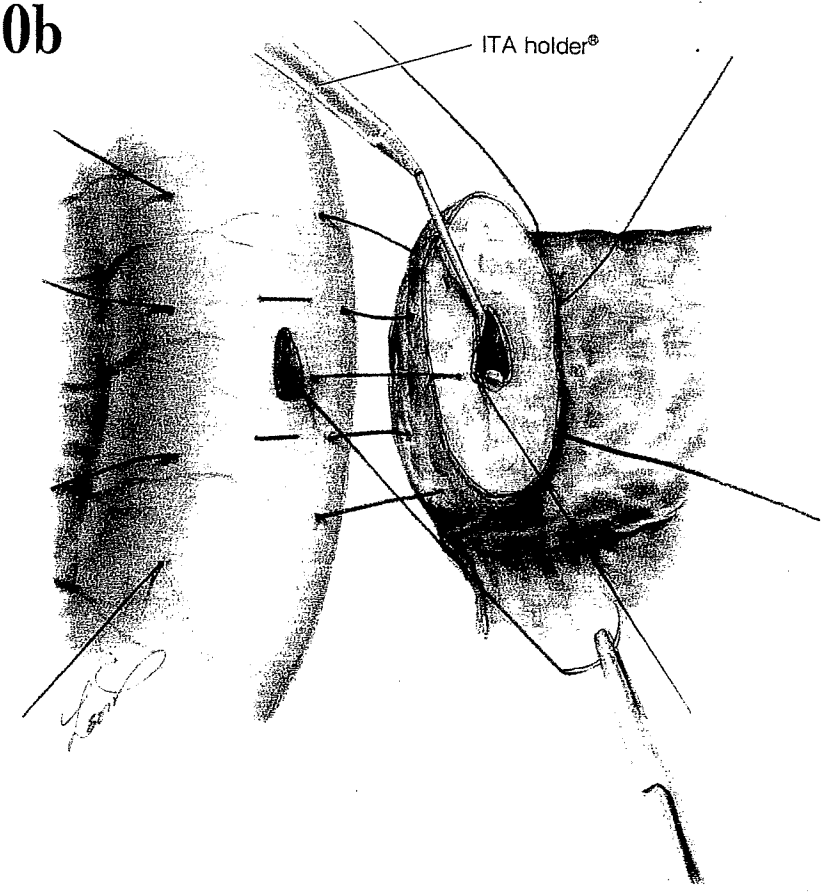
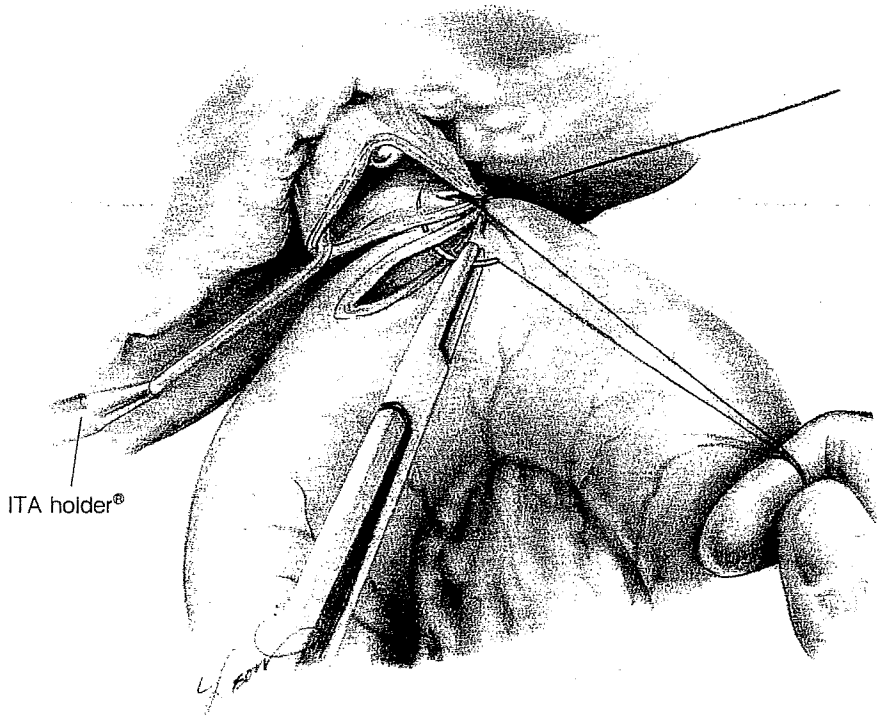


図10　膵管空腸吻合

当科では柿田法変法を行っている。膵実質と空腸の漿膜筋層との間の密着吻合を 4-0 Prolene 糸で３～４針，膵管粘膜吻合を 5-0 PDS 糸で８針縫合する(a)。膵実質の損傷を防ぐために膵実質を把持せず ITA holder® を用いて膵管空腸吻合の運針を行う (b)



11. 閉腹まで

吻合終了後，腹腔内を生理食塩液3 *l* 以上で洗浄し，止血を最終確認する。閉鎖吸引式ドレーンを右側腹部よりWinslow孔を通して膵空腸吻合背側に1本，そして左側腹部より胃空腸吻合背側を通して膵空腸吻合背側に留置する。正常膵症例では，経腸栄養カテーテルを左側腹部より体外に誘導し，腸壁と腹壁を4針で固定する。さらに温存した大網を膵空腸吻合部の下面から背側に誘導し，吻合部に巻きつけるよう吻合部腹側に固定する（図12）。腹壁を3層に閉鎖する。

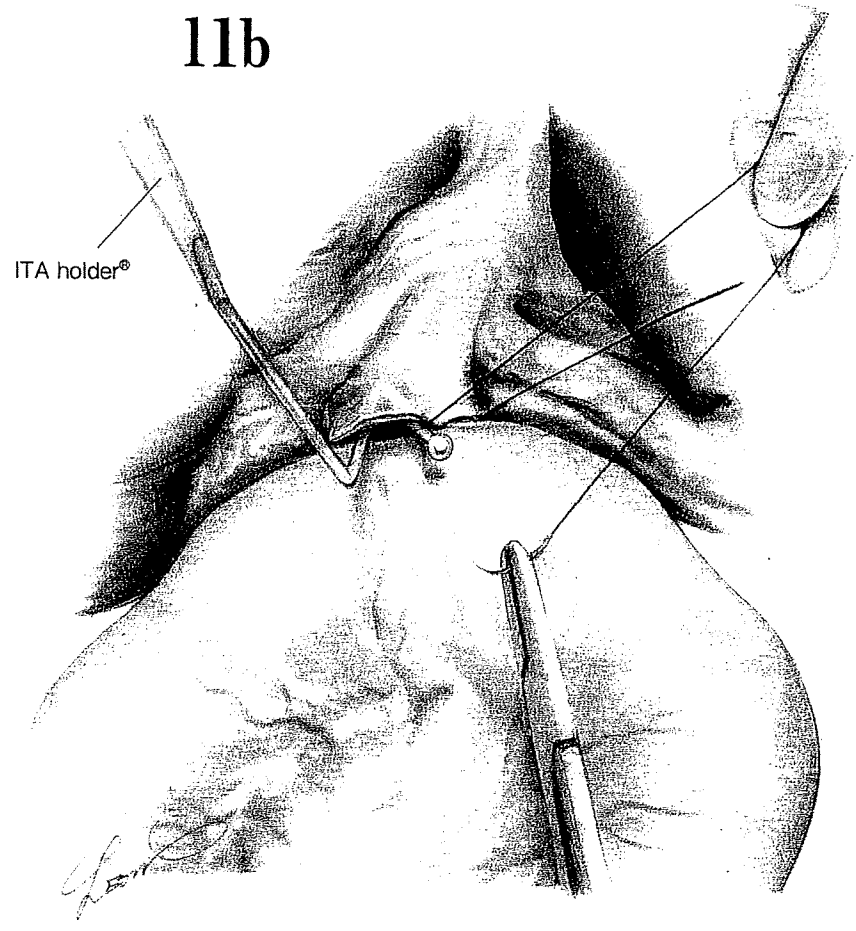


図11　胆管空腸吻合
4-0 PDS 両端針を用いた連続縫合を行い，膵管空腸吻合と同様に ITA holder® を用いて後壁から（a），前壁へと順に吻合を行う（b）

12

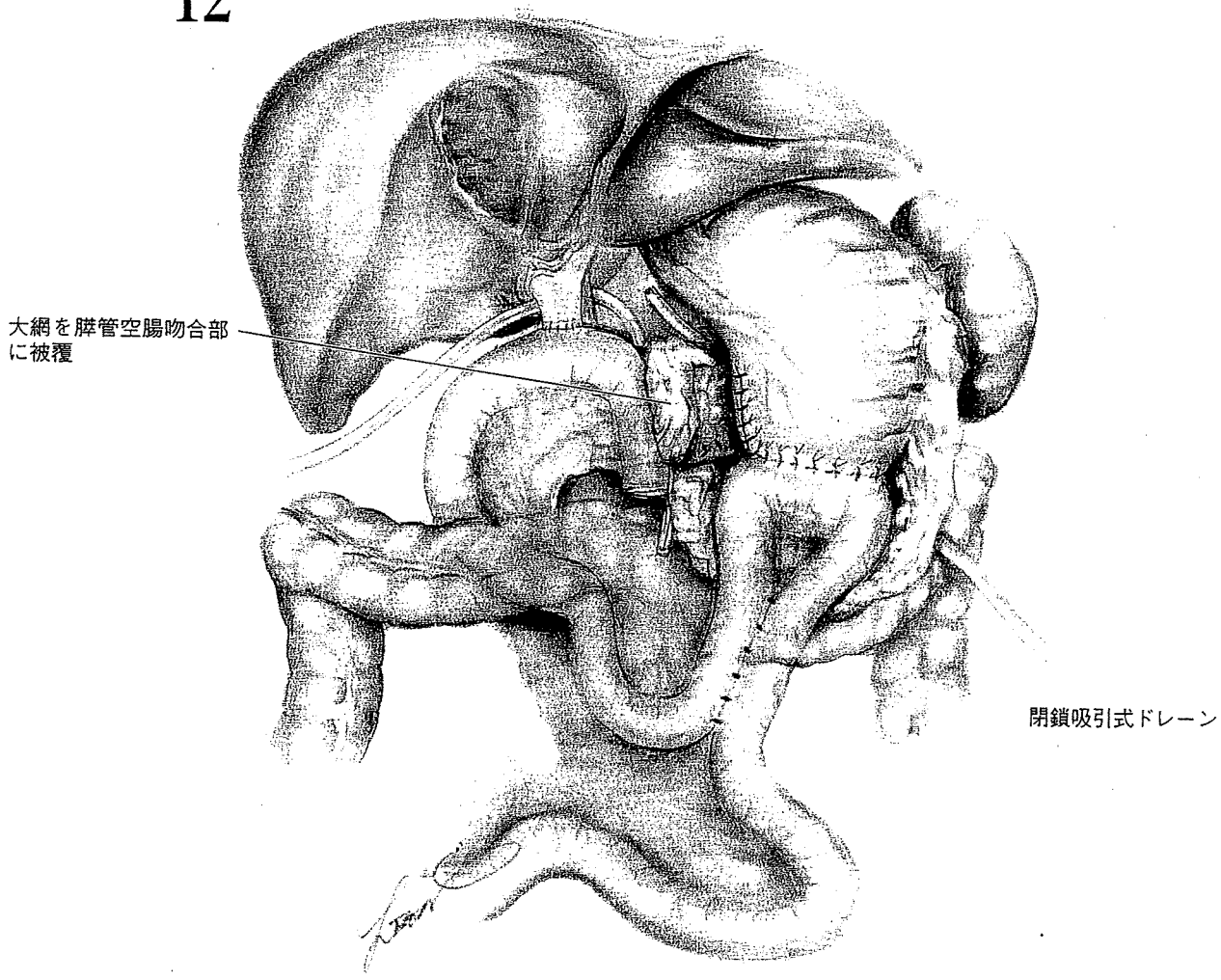


図12　膵空腸吻合部への大網の被覆とドレーン留置
ドレーンは閉鎖吸引式ドレーンを右側腹部よりWinslow孔を通して膵空腸吻合背側に1本，左側腹部より胃空腸吻合背側を通して膵空腸吻合背側に留置する。保存した大網を膵空腸吻合部の下面から背側に誘導し，吻合部に巻きつけるよう吻合部腹側に誘導し固定する

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〔Expanded Abstract〕

膵頭十二指腸切除術後合併症を低減させるための新指針

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背景と目的

外科技術の向上や周術期管理の改善により，(幽門輪温存) 膵頭十二指腸切除術 (以下 PD) の死亡率や合併症率は軽減してきた．多くの high volume center における PD の死亡率は 5% 以下となってきたが，合併症率は依然 40% 前後と高率である[1]．われわれの施設における過去の連続 198 例の PD の成績は，死亡率 5.5%，合併症率 56% であり，多くの合併症は膵液漏の存在と強く関連していた[2]．われわれは，2004 年 6 月以降，新指針を用いて膵腸吻合法や周術期管理を変更した 51 例 (膵腸吻合を柿田法[3]変法に変更し大網ラッピング，閉鎖吸引式ドレーンの早期抜去，胆管・膵管外瘻術の制限) と，それ以前の 77 例の合併症率を比較検討したので報告する．

方　法

2000 年 1 月から 2006 年 8 月までの連続 128 例を対象とした．2000 年 1 月から 2004 年 5 月までの 77 例は，膵空腸吻合を嵌入法で行い，膵管や胆管不完全外瘻術を付加した．腹腔ドレーンは 10 mm のペンローズドレーンを少なくとも術後 6 日間留置した (A 群)．2004 年 6 月から 2006 年 8 月までの 51 例 (B 群) を対象に膵腸吻合法や周術期管理を以下のように変更した．①嵌入法から柿田法[3]変法に変更，②膵腸吻合部に Omental wrapping を付加，③閉鎖吸引式ドレーンの早期抜去，④膵管や胆管外瘻術の制限 (膵管径 3mm，胆管径 10mm 以下)．国際診断基準[4]を基に膵液漏を規定し，A・B 群間で合併症率を比較し，多重回帰分析を用いて合併症に対する危険因子の同定を行った．

結果と考察

膵液漏を予防するための取り組みとしての膵腸吻合法には多くの報告があるが，膵管空腸粘膜吻合法の導入は，1945 年 Varco[5]らにより始まり，1996 年に Kakita[3]らが，安全かつシンプルな方法として柿田法を紹介した．これは，膵管空腸粘膜吻合を 3～4 針の結節縫合 (膵管ステント留置) と膵実質と空腸の密着縫合 (6～8 針の結節縫合) からなる方法で，密着縫合により膵と空腸間の死腔が形成されないこと，膵実質に少数の縫合糸を用いて吻合を行うため膵断端の虚血や壊死が防止されることにある．われわれは，膵管空腸粘膜吻合をより確実に行い，膵実質への運針をさらに減らすために，柿田法を基本として，膵管空腸粘膜吻合に 8 針結節縫合を，ならびに膵空腸密着吻合に 3～4 針運針する方法を行い，柿田法変法とした．従来の嵌入法では，膵実質 (断端) と空腸の間に 10～30 針の運針を行い，それらを結紮する際に膵損傷の危険性が高いと考えられてきたが，柿田法変法では膵実質への運針数が比較的少なく，膵損傷の危険性が低下すると考えられる．また Omental wrapping を付加することによる膵液漏関連合併症，閉鎖吸引式ドレーンの早期抜去による腹腔内感染症，そして膵胆管外瘻術の制限による手術部位感染が低減することが期待された．

本研究において，背景因子の比較に関して，A 群で膵管や胆管外瘻留置率や同種輸血率が有意に高率であったが (Table 1，$p<0.0001$)，疾患比率，膵管径や手術方法などに有意な差は検出されなかった．術後合併症率の比較において，膵腸吻合法や周術期管理の変更により，Grade B/C の膵液

Table 1 Patients' Characteristics

Parameters	Group A	Group B	*p* value
· Pancreaticojejunostomy	invagination	modified－Kakita	
· Omental wrapping	none	done	
· Drain	open	closed－suction	
· Criteria of drain removal	none	done	
· Pancreatic duct diameter (≥3mm : <3mm)	49 : 28	35 : 16	n.s.
· pancreatic duct drainage (+ : −)	75 : 2	16 : 35	< 0.0001
· bile duct drainage (+ : −)	76 : 1	13 : 38	< 0.0001
· Age (y)	65 (47－83)	68 (51－84)	n.s.
· Male : female	42 : 35	33 : 18	n.s.
· Disease (P : B : A)	42 : 20 : 15	29 : 9 : 13	n.s.
· Benign : malignant ratio	4 : 73	4 : 47	n.s.
· Total Bil (mg/dl)	0.8 (0.3－5.6)	0.7 (0.3－4.7)	n.s.
· AST (U/l)	27 (12－132)	24 (12－77)	n.s.
· Amylase (U/l)	73 (8－404)	70 (11－473)	n.s.
· Albumin (g/dl)	3.7 (2.3－4.6)	3.7 (2.3－4.5)	n.s.
· WBC ($\times 10^2$/ml)	48 (16－154)	50 (31－98)	n.s.
· Hb (g/dl)	11.6 (8.5－15.4)	11.6 (8.3－14.1)	n.s.
· Co－morbid disease (+ : −)	28 : 49	19 : 32	n.s.
· DM (+ : −)	43 : 34	32 : 19	n.s.
· Jaundice (+ : −)	60 : 17	33 : 18	n.s.
· CRT (+ : −)	16 : 61	7 : 44	n.s.
· Type of op (PD : PpPD)	53 : 24	33 : 18	n.s.
· Operation time (min)	545 (300－905)	523 (355－795)	n.s.
· Blood loss (ml)	1170 (375－7250)	1140 (212－6420)	n.s.
· Transfusion (allo : auto : none)	39 : 12 : 26	16 : 30 : 5	< 0.0001
· Resection of other organs (+ : −)	13 : 64	7 : 44	n.s.
· Food intake (≤POD－7th vs >8)	14% : 86%	67% : 33%	< 0.0001
· Day of drain removal (≤POD－6th vs >7)	1% : 99%	53% : 47%	< 0.0001

Table shows median value (range) or number of patients.

P : B : A, pancreatic disease : biliary disease : ampullary disease; Bil, Bilirubin; AST, aspartate aminotransferase; WBC, white blood cell count; Hb, hemoglobin; DM, diabetes mellitus; CRT, preoperative chemo－radiation therapy; PD, pancreaticoduodenectomy; PpPD, pylorus preserving pancreaticoduodenectomy; allo, allogenic blood transfusion; auto, autologous blood transfusion; none, no transfusion; food intake (≤POD－7th vs >8), food intake was initiated within post－operative day－7th vs over post－operative day－8th.

Table 2 Comparison of post-operative complications

Parameters	Group A	Group B	*p* value
· overall complications	49/77 (64%)	20/51 (39%)	0.0109
· septic complication	23/77 (30%)	10/51 (20%)	n.s.
· re-operation	4/77 (5.2%)	1/51 (2.0%)	n.s.
· in-hospital death	0/77 (0%)	1/51 (2.0%)	n.s.
· pancreatic fistula	21 (27%)	7 (14%)	0.0828
Grade A : B/C	6 : 14/1	4 : 3/0	0.0376
· DGE	18 (23%)	3 (6%)	0.0133
· drain infection	4 (5.2%)	3 (5.8%)	n.s.
· abdominal abscess	7 (9.1%)	2 (3.9%)	n.s.
· hemorrhage	1 (1.2%)	0 (0%)	n.s.
· wound dehiscence	22 (29%)	10 (20%)	n.s.
· pneumonia	1 (1.3%)	1 (2.0%)	n.s.
· bile leakage	1 (1.3%)	1 (2.0%)	n.s.
· marginal ulcer	10 (13%)	1 (2.0%)	n.s.
· peritoneal/pleural effusion	14 (18%)	6 (12%)	n.s.
· GJ leakage	2 (2.6%)	0 (0%)	n.s.
· GJ stricture	4 (5.2%)	0 (0%)	n.s.
· liver dysfunction	10 (13%)	4 (7.8%)	n.s.

Figure represents number of patients (%).
DGE : delayed gastric emptying, fluid collection : pleural effusion or/and ascites, GJ : gastro-jejunostomy.

漏（19% から 6%）は有意に低率となり，胃内容排泄遅延（23% から 6%）や全合併症発生率の有意な低下（64% から 39%）が認められた（Table 2, $p<0.05$）．さらに，合併症率の低減や周術期管理の変更が，ドレーン抜去日の短縮や早期の経口摂取開始に関連したと考えられた．多重回帰分析により，柿田法変法の導入が，全合併症率，膵液漏（grade B/C）や胃内容排泄遅延の発生率低減に有用であった．

まとめると，柿田法変法をはじめとする周術期管理の新指針は，全合併症，Grade B/C 膵液漏，胃内容排泄遅延発生率の低減に関連し，安全な PD 施行に有用であると考えられた．

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〔Expanded Abstract〕

膵管癌に対する術前放射線化学療法後外科的治療成績

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背景と目的

膵癌に対する外科的切除術は，唯一の根治的治療であるものの，早期に再発転移しその長期予後は不良であることから，切除単独治療の限界が示唆される．Traverso[1]は，膵癌患者の5年生存率を50％超に到達せしめる条件として，正確な術前診断による適切な患者選択，過不足ない手術，high-volume centerでの集中治療，効果的な術前後の補助治療の導入を提唱している．

術前治療の中でも術前放射線化学療法（NACRT）後の切除は，適切な患者選択と根治切除率を増加し，リンパ節転移率や局所再発率を低下させると報告されている[2~5]．

そこで今回，われわれは，NACRT後切除例と切除単独例の間で，累積生存率（OS），無再発生存率（DFS）や初回再発形式を比較検討した．

方　法

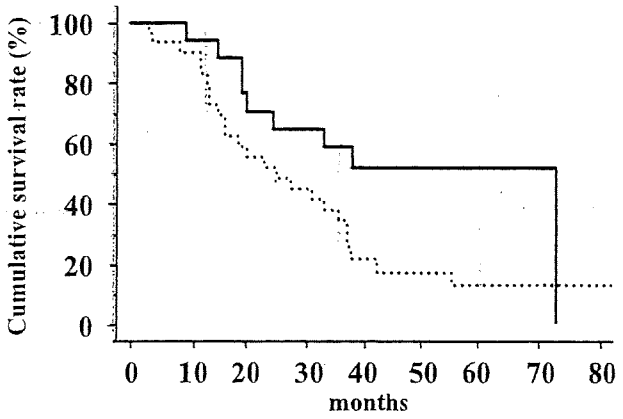
2000年1月から2005年12月までに臨床的に膵癌と診断した連続175例の内，切除を行った通常型膵癌68例を対象とした．2001年から2004年までに，画像上TNM分類におけるT3/T4症例の35例に対してNACRT（体外照射40Gy＋low dose 5FU＋CDDP；n＝13 or Gemcitabine 400 mg/m^2 3投1休；n＝22）を行い，切除を施行した27例をNACRT群とした．一方でほぼ同時期に切除のみを行った41例を切除単独群として，腫瘍因子，OS，DFSを比較検討した．さらに，外科的根治切除例の成績も同様に比較した．全ての症例は，補助化学療法を施行せず，切除後最低25ヶ月間経過観察を行った．

結果と考察

Craneら[2]は，術前放射線化学療法（NACRT）の利点として，治療経過中に急速に腫瘍進展を示す症例を除外でき患者選択に有用であること，良好な忍容性，切除による放射線晩期障害の予防などを指摘している．一方でNACRTの欠点として，Tseら[3]は，早期膵癌や良性膵腫瘍に対する過剰治療の可能性に言及してきた．

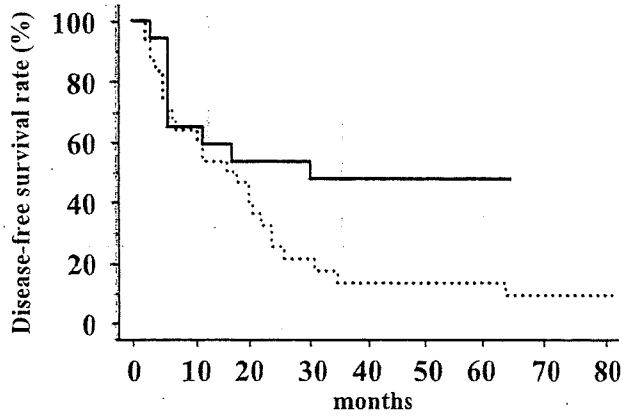
本研究において，NACRT群では治療期を通じて23％の症例が非切除となり，最終的に77％（27/35）に切除を行った．NACRT群27例では，切除単独群41例と比較してリンパ節転移率が有意に低く（32％ vs 59％，p＝0.044），組織学的根治切除率が有意に高率であった（52％ vs 22％，p＝0.004）．次に両群間の外科的根治切除例のOSの比較でも，NACRT群18例は切除単独群30例と比較して有意に予後良好であった（1，3，5年生存率，NACRT：94，59，52％ vs 切除単独：83，34，13％，p＝0.0425，Fig. 1）．さらにDFSの比較においても，1年以内は両群とも同様であったが，その後は経時的に開大がみられ，NACRT群で有意に良好であった（p＝0.0359，Fig. 2）．初回再発部位の検討では，両群間で遠隔転移率は同等であったが，NACRT群の局所再発率は11％と，切除単独群の47％と比較して有意に低率であった（p＝0.0024）．

MD Anderson Cancer CenterのEvans[4]は，Gemcitabine-baseの放射線化学療法後切除を行い，33ヶ月の生存期間中央値（MST）を得たことを報告している．また，Talamontiら[5]も，full-dose



patients at risk		1y	2y	3y	4y	5y	MST
NACRT	18	16	12	8	5	4	-
surgery alone	30	25	15	8	4	2	24 m

Fig. 1　術前放射線化学療法群と切除単独群間の累積生存率の比較（根治切除例）
実線は術前放射線化学療法群（n = 18）で，破線は切除単独群（n = 30）間の生存曲線を示す．両群間に統計学的有意差が認められた（p = 0.0425）．



patients at risk		1y	2y	3y	4y	5y
NACRT	18	10	9	7	4	3
surgery alone	30	16	8	3	2	2

Fig. 2　術前放射線化学療法群と切除単独群間の累積無再発生存率の比較（根治切除例）
実線は術前放射線化学療法群（n = 18）で，破線は切除単独群（n = 30）間の無再発生存曲線を示す．両群間に統計学的有意差が認められた（p = 0.0359）．

Gemcitabine の多施設共同 Phase II 試験の結果より，MST が 26 ヶ月であったと報告している．NACRT は，単施設からの報告をみる限り非常に魅力的であるが，ランダム化試験が行われていないことが問題点である．

まとめると，膵癌に対して NACRT を行い，根治切除例では生存率の改善がみられた．膵癌の 5 年生存率 50% 超を達成するためには，より効果的で副作用の少ない術前治療のレジメを確立してその成績を検証していく必要があると考えられた．

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Expanded abstract cited from the original paper:

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特集 長期生存膵癌の条件

膵癌術後長期生存を得るための集学的治療戦略

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Multi-Disciplinary Management for Obtaining Long-Term Survivors in Patients with Pancreatic Cancer: Satoi S*1, Toyokawa H*1, Yanagimoto H*1, Kitade H*1, Sonte Kim*1, Yamao J*1, Yamamoto T*1, Hirooka S*1, Matsui Y*1 and A-Hon Kwon*1 (*1Department of Surgery, Kansai Medical University)

We explored the outcome of the multi-disciplinary management for obtaining long-term survivors in patients with pancreatic cancer that extended beyond the pancreas. Our experiences of surgical resection following the pre-operative chemoradiation (pre-CRT) therapy showed that pre-CRT could be associated with a lower rate of lymph node metastasis and a higher rate of R0 resection, resulting in improved prognosis of patients with pancreatic cancer that extended beyond the pancreas.

Key words: Pre-operative chemoradiation, Curative resection, Lymph node metastasis, Overall survival rate, Disease-free survival rate

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はじめに

膵癌は解剖学的特殊性ならびに高い生物学的悪性度から容易に周囲組織に浸潤性進展をきたし，早期に遠隔臓器に転移することが特徴である．外科的治療が唯一の根治性を追及する方法であるが，膵癌切除例の5年生存率は10%前後と予後不良である[1,2]．このことは，膵癌に対する切除単独治療の限界を示唆しているとも考えられる．

今回われわれは，当科における膵癌の治療経験に基づき，膵癌切除例の長期予後を改善するための進展度診断と治療戦略の工夫を提示する．

*1 関西医科大学外科

1 術前進展度診断

切除により恩恵を受ける症例を適切に選択することが，膵管癌の術前進展度診断のために必要不可欠であり，特に肝転移の有無と血管浸潤の程度が治療内容の選択に大きな影響を与えると考えられる．

2000年から2002年8月まで血管造影下CT（7 mm slice CTHA/CTAP）で行い，2002年9月以降はcine-imaged MDCT（以下MDCT）を使用してきた．MDCTは，動脈相と門脈相を撮像し，検出器構成1.25 mm（4, table移動3.75 mm/rotation，ヘリカルピッチ3のHigh quality (HQ) modeで，横隔膜下肝臓の高さから腎下縁までスキャンし，スライス厚1.25 mm，再構成間隔0.6 mmの画像を再構成して，このデータをワークステーションへ転送した．動脈相と門脈相

のデータからvolume dataを再構成し，軸位・冠状断・矢状断の画像を作成した上でシネ画像として繰り返し観察した．MDCTと従来法であるCTHA/CTAP/angiography/CECTの両者を用いて，術前進展度診断を行い，肝転移の正診率や，術前CTにおける腫瘍因子の外科的，病理学的腫瘍因子との整合性を比較検討してきた[3]．肝転移の正診率はMDCTで高く，特に10 mm以下の腫瘍性病変はCTHA/CTAP/angiography/CECTに比較して高率に診断可能であった．また，門脈や動脈浸潤の手術所見との整合性を比較すると，MDCTはCTHA/CTAP/angiography/CECTと比較して外科的血管浸潤をより正確に反映していた．しかしながら，MDCTによる術前進展度診断を行い切除可能と診断された症例で，開腹時に予期せぬ遠隔転移症例が約10%にみられたことが問題であり，特に術前治療における患者選択に大きな影響を与えうる問題と考えられた[4]．

2 術前化学放射線療法の治療成績

当科における膵癌の画像上の切除基準は，膵頭部領域では，腫瘍が総肝動脈や上腸間膜動脈と半周以上で接していないこと，門脈進展があっても，完全閉塞に伴う側副血行非形成例で根治切除が可能と考えられる場合としている．膵体尾部領域では，癌が腹腔動脈幹に浸潤していても上腸間膜動脈や胃十二指腸動脈に浸潤していなければ，積極的に腹腔動脈幹合併切除を行っている．

2000年から2005年までに経験した膵癌に対して外科的切除を施行した連続68例を対象としてその成績を検討した．画像上膵外に連続進展を示す膵癌35例（膵癌取扱い規約[5]のT3一部とT4）に対して術前化学放射線療法を行った．再評価により全例でradiological responseは認められず，8例が切除不能となり（23%），最終的に切除27例（Neoadjuvant chemoradiation: NACRT群）と，ほぼ同時期の切除単独群41例の治療成績をretrospectiveに比較検討した．これらの結果はすでに報告しているが[6,7]，今回の報告では観察期間を最低39カ月間（生存例では48カ月間）に延長して生存率を比較検討した．術前化学放射線療法は，全例に40 Gyの非原体照射（2 Gy/日×5日/週，4週間）を施行した．併用化学療法は13例にCDDP＋5FU療法を，22例に塩酸ゲムシタビン（GEM）400 mg/m^{2}を3投1休で投与した．5-FUは200 mg/m^2/日を5日/週で計20日間の持続投与を行い，CDDPは1週目に3 mg/m^2/日を5日間bolus投与し，以降の3週間は6 mg/m^2/日を週2日間投与し，計11回投与とした．両群とも再発・転移診断時には化学療法が行われたが，術後補助化学療法は施行されなかった．

両群間の背景因子に差はなかった．NACRT群では，切除単独群と比較してリンパ節転移率が有意に少なく（32% vs 59%, $p<0.05$），R0率が有意に高率であった（52% vs 22% $p=0.004$）．図1に示すように，NACRT群の累積生存率は，切除単独群と比較して良好な傾向であった（$p=0.0541$）．次に図2に示すように，癌遺残度のR0/1症例において，NACRT群（n＝18）は切除単独群（n＝30）と比較して有意に予後良好であった．さらに図3に示すように無再発生存率もNACRT群で有意に良好であり，1年以内の再発は両群とも同様であったが，その後は経時的に開大がみられ，4年間の観察期間で，最終的にNACRT群では7例（39%）が無再発生存で，切除単独群では2例（7%）が無再発生存で1例が再発生存であった（$p<0.05$）．実5年生存例は切除単独群で3例のみであったのに対して，NACRT群では5例であり，さらに3例が4年以上生存している．

1988年より術前放射線化学療法を行っているMD Anderson Medical CenterのEvansら[8]は，86例のpotentially resectable膵癌に対してGEM 400 mg/m^2，週1回を7週間投与し，同時に30 Gyの対外照射を行った結果，74%が切除可能で，その実5年生存率は36%と報告した．これは，potentially resectable膵癌50例以上で5年以上観察しえたNACRT後切除成績の唯一の報告である．われわれの成績は，症例数が少なく化学療法剤が異なるため解釈には注意が必要であるが，Evansら[8]の成績と同様に約20%に遠隔

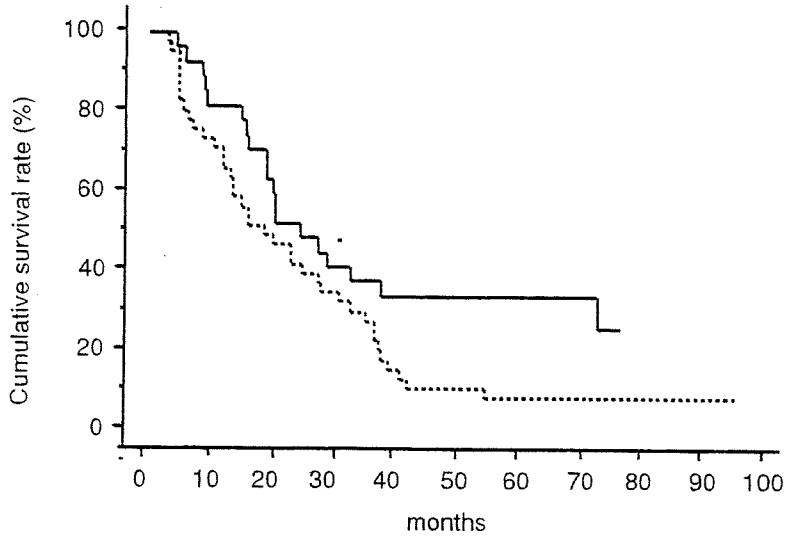

図1　術前化学放射線療法施行後切除27例（NACRT群）と切除単独群41例の累積生存曲線の比較（実線はNACRT群，破線は切除単独群を示す）

NACRT群の累積生存曲線は，切除単独群と比較して良好な傾向であった（p＝0.0541）．NACRT群の実4年生存率は30%であり，切除単独群は9.8%であった．

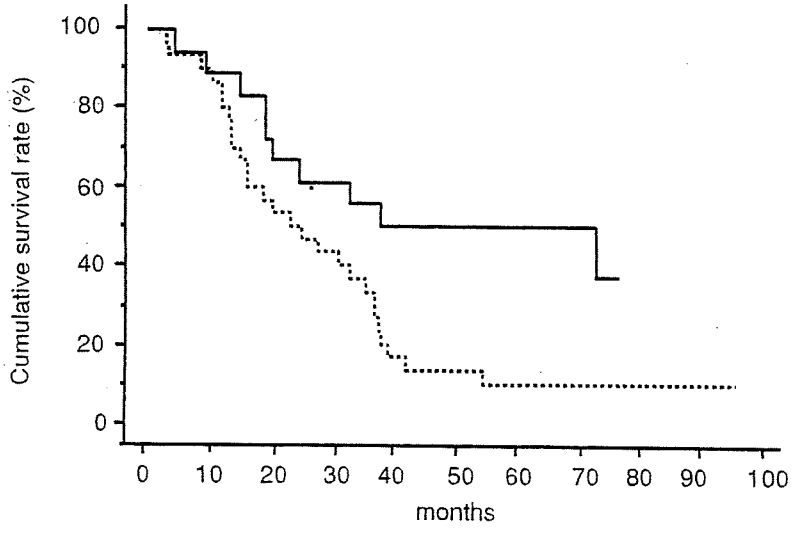

図2　根治切除例（R0/1）の累積生存曲線の比較：NACRT群18例と切除単独30例（実線はNACRT群，破線は切除単独群を示す）

NACRT群根治切除例の累積生存曲線は，切除単独群と比較して有意に良好であった（p＝0.0253）．NACRT群の実4年生存率は43%であり，切除単独群は13%であった．

転移などで切除不能例があるものの，切除されたNACRT群では，切除単独群と比較してリンパ節転移率が低く，根治切除率（R0）が高く，局所再発率が低率であった．結果的に無再発生存率と生存率が良好であり，NACRT群では実4年生存率が50%という良好な成績を示した．

3 新たなる取り組み

今回報告した術前化学放射線療法後切除例の成績は良好であったが，切除前に約20%の症例が脱落していること，今回の化学療法剤ではradiological responseがみられなかったこと，術後1

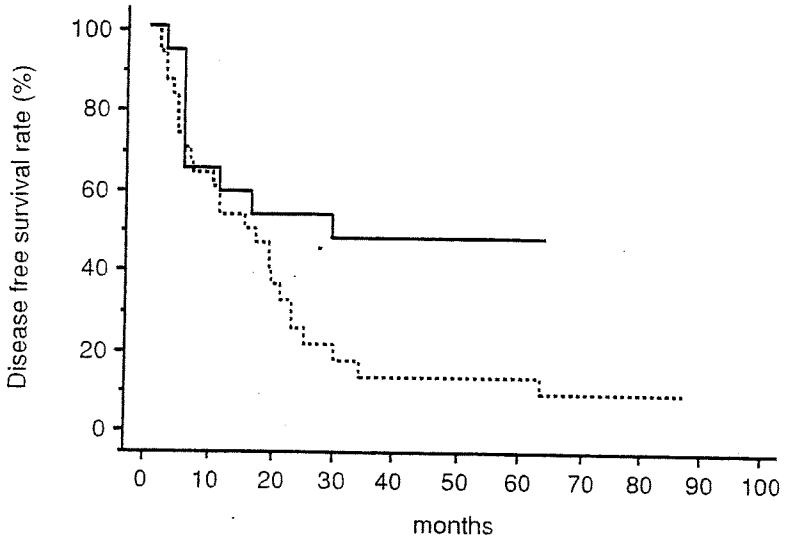

図3　根治切除例（R0/1）の累積無再発生存曲線の比較：NACRT群18例と切除単独30例（実線はNACRT群，破線は切除単独群を示す）
NACRT群の累積無再発生存曲線は，切除単独群と比較して有意に良好であった（p=0.0359）.

年以内の再発率が約50%と不良であること，が問題点として挙げられる．術前化学放射線療法を施行し切除不能であった8例の成績をみると，生存期間中央値は5.5カ月で1年以上生存した症例は皆無であった．これらの症例では化学放射線療法施行前よりCT画像では捉えきれない微小肝・腹膜転移が存在していた可能性も否定できない．実際，CTの質にもよるが，局所進行膵癌の開腹非切除率は20～57%といわれており，膵癌症例では微小肝腹膜転移の潜在的リスクを考慮する必要がある[9].

これらの問題点を克服するために，われわれは，2008年度より術前化学放射線療法後脱落例を低減するために全例にstaging laparoscopyを行い患者選択を行った上で，当科における切除可能例を対象に，TS1を使用した化学放射線療法を行っている．

実際staging laparoscopyでは，微小肝転移（特に肝表面）や腹膜転移の検出率が高く，さらに超音波検査や血管浸潤同定のための剥離操作を加えるとさらにその正確性は増すといわれている[9]．われわれの施設での経験では，2006年から2008年の切除不能な局所進行膵癌30例に対してstaging laparoscopyを施行した結果，59%に微小遠隔転移を認めたことより，術前化学放射線療法対象患者全例にstaging laparoscopyを施行して遠隔転移例を積極的に除外している．

次に，膵癌に対する新規抗がん剤であるTS1と放射線治療の併用療法に関して，本邦より3件のPhase I試験の結果[10～12]が示されており，その安全性と19～43%のpartial responseが確認されている．さらに最近，韓国のKimら[13]により切除不能膵癌に対するPhase II試験の結果が報告され，partial responseが24%で生存期間中央値が13カ月という良好な成績が示された．TS1を使用した放射線治療を行うことにより腫瘍縮小効果と予後の改善がさらに期待される．また，切除例においては術後の補助化学療法を施行し，再発率の低下を期待している．

まとめると，過去の術前治療で得られた問題点である治療前診断，低い腫瘍縮小効果，術後早期転移の問題点を克服するために，2008年度より術前進展度診断にcine-imaged MDCTを行い切除可能と診断された膵外進展を示すT3/4症例（膵癌取り扱い規約）に対して，微小肝腹膜転移診断のためにstaging laparoscopyを全例に行い，無遠隔転移例を対象にTS1　100 mg/m^2＋50.4 GyのNACRTを行い，3週間後に再評価を行った上で，進行例を除いて切除を行い，補助化学療法を追加するPhase II試験を行っている．

予定症例数は30例で，手術終了後の根治切除率と有効性および安全性を確認することを目的として，現在症例集積中である．

まとめ

難治性膵癌の外科治療において，術前のより正確な進展度診断を行い，適切な患者選択のもと，放射線化学療法後に再評価して切除を行うことにより，長期予後が改善される可能性がある．今後，多施設での切除単独例との比較試験や術前化学療法との比較などを行い，術前放射線化学療法の治療効果を明らかにしていく必要がある．

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Original Paper

Pre-Operative Patient Selection of Pancreatic Cancer Patients by Multi-Detector Row CT

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ABSTRACT

Background/Aims: Accurate pre-operative staging in patients with pancreatic cancer is crucial for avoiding unnecessary laparotomy and for selecting patients accurately for curative resection. In this study, tumor resectability and residual tumor grading in patients evaluated by MD-CT (Multi-detector row CT) or by SD-CT (single-detector CT) were compared to determine whether more accurate imaging has a significant clinical impact on patient selection and surgical outcomes.

Methodology: One hundred-fifty consecutive patients with pancreatic cancer evaluated from January 2000 to April 2005 were included in this retrospective study. Seventy pancreatic cancer patients underwent pre-operative evaluation using SD-CT and angiography (5-7 mm slice thickness, 1st period 2000-2002), and 80 patients underwent MD-CT (1.25 mm slice thickness, 2nd period 2002-2005).

Results: The introduction of MD-CT had a significant impact on the selection of suitable patients, this group showing a lower frequency of surgical intervention in cases of incurable disease (p=0.0383). Pre-operative evaluation using MD-CT in the resected cases also provided a higher percentage of accurate R0/R1 grading relative to SD-CT evaluations (p=0.0164).

Conclusion: MD-CT imaging has a significant impact on preventing unnecessary exploratory surgery and on the selection of appropriate pancreatic cancer patients for surgical resection.

KEY WORDS: Resectability; Potentially resectable tumor; Incurable tumor; Unresectable tumor; Grading of residual tumor; Overall survival rate; Disease-free survival rate; CTHA, CTAP; Angiography.

ABBREVIATIONS: CT During Hepatic Arteriography (CTHA), CT During Arterioportgraphy (CTAP)

INTRODUCTION

Pancreatic cancer is a lethal disease with poor prognosis. Even after radical operation, the five-year survival rate varies between 10-30% (1-4). At the time of pancreatic cancer diagnosis, only 15-20% of patients have potentially resectable disease without evidence of major vessel involvement or distant metastases (5). For these cases, surgical resection remains the only potentially curative treatment. Since the management of patients with incurable disease should be primarily non-surgical, it is essential to select patients who may benefit from surgery by staging cancers accurately. Relapsed disease, particularly at an early post-operative phase, can also affect surgical outcome adversely in pancreatic cancer patients. Underestimation of pre-operative tumor extension, inability to perform surgical clearance of the tumor, and biological features of the tumor all can contribute to early relapse of the tumor, even in patients who have undergone curative resection.

We reported previously that the accuracy of multi-detector row CT (MD-CT) for detection of pancreatic cancer liver metastasis or vascular involvement was superior to single detector (SD) CT (6). Between 2000 and 2002, SD-CT and abdominal angiography were used routinely for pre-operative staging. In September 2002, we began applying MD-CT for pre-operative evaluation of pancreatic cancer patients. In addition to the superior spatial resolution of MD-CT and the possibility of multi-planar reconstructions, MD-CT images with thinner collimation provide more accurate and detailed information than images from conventional contrast-enhanced CT (7,8). We hypothesized that using MD-CT to improve the accuracy of liver metastasis and vascular invasion diagnoses would reduce the frequency of unnecessary laparotomy, resulting in improved surgical results for eligible pancreatic cancer patients.

The goal of this study was to compare tumor respectability and residual tumor grading between patients examined before or after the introduction of MD-CT.

METHODOLOGY

One hundred-fifty consecutive patients with ductal adenocarcinoma of the pancreas that were evaluated between January 2000 and April 2005 in Kansai Medical University Hospital were included in the study (**Table 1**). After clinical diagnosis of pancreatic cancer using ultrasonography, CT, MRCP, ERCP, endoscopic ultrasonography, cytological examination of the bile juice and/or biopsy of the bile duct mucosa

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(conducted at the Department of Gastroenterology), all patients were referred to the Department of Surgery for pre-operative evaluation of tumor extension. Pre-operative staging was focused on (1) the detection of liver or lymph-node metastases, (2) identifying tumor vascular involvement, and (3) obtaining information about the anatomy of the celiac trunk and superior mesenteric arteries. Cases involving an endocrine tumor of the pancreas, intraductal papillary mucinous cancer, acinar cell cancer, or anaplastic cancer were excluded.

Patients in the study were classified according to radiological results into one of four groups: "incurable", "locally advanced", "potentially resectable", and "unresectable". "Incurable" cases involved diagnosis of peritoneal carcinomatosis or distant organ metastasis. "Locally-advanced" cases consisted of patients without any distant organ metastasis, but with (1) vascular involvement of a major peripancreatic artery (defined as tumor in-growth with >50% vessel contiguity in the celiac trunk, common or proper hepatic artery or superior mesenteric artery), (2) extended obstruction of the portal vein to distal branches of the superior mesenteric vein, or (3) with cavernous transformation of the porta hepatic. At the time of laparotomy, patients demonstrating tumors with any of the features above were classified as "unresectable" and were not treated surgically. Patients with no distant organ metastasis or tumor extension to a major peripancreatic artery [as defined in (1)] were classified into the "potentially resectable" group. Patients with tumors that invaded the portal vein were also classified as candidates for surgical resection but only in the absence of extended obstruction of the portal vein to distal branches of the superior mesenteric vein, or cavernous transformation of the porta hepatis. Patients with cancer in the pancreatic body and tail, with celiac trunk invasion and without SMA invasion, were classified as "potentially resectable" candidates for curative resection.

Table 1. Patient Characteristics

	1st term	2nd term	*p* value
Time	2000.1-2002.8	2002.9-2005.4	
Number of patients	70	80	
Age	64 (47-82)	65 (39 - 83)	n.s.
Gender (Male : Female)	31 : 39	37 : 43	n.s.
Incurable cases	27 (39%)	48 (60%)	0.0138
Reason (local:distant)	8:19	10:38	n.s.
Potentially resectable cases	43 (61%)	32 (40%)	0.0138
Resected cases	33 (47%)	29 (36%)	n.s.
R0 (%)	6 (18)	15 (52)	0.0164
R1 (%)	13 (39)	8 (28)	
R2 (%)	14 (43)	6 (20)	
Unresected cases	10 (14%)	3 (4%)	0.0383
Reason (local:distant)	2:8	0:3	n.s.

Unresectable case: patients who had no indication for surgical resection on laparotomy. Incurable case: patients who had no indication for laparotomy due to detection of distant metastasis and/or locally advanced tumor during pre-operative radiological examination. Local, locally advanced disease; distant, distant metastasis. R0, negative margin; R1, positive microscopic margin; R2, positive gross margin

The following strategy was basically applied for treatment of the remaining pancreatic cancer patients: Patients with potentially resectable cancer underwent only surgical resection, primarily. Patients with locally advanced cancer received chemo-radiation (possibly followed by surgical resection), and patients with distant organ metastasis received systemic chemotherapy. MD-CT or SD-CTs/angiography was performed for tumor staging at least two weeks before surgery, chemotherapy or chemo-radiotherapy. Informed consent from each patient included in the study was obtained in accordance with the provisions of the Declaration of Helsinki. Patient data were obtained from the prospective database of Pancreatic Disease at Kansai Medical University Hospital.

MD-CT was used to evaluate 80 patients with pancreatic cancer from September 2002 to April 2005 (2nd term). Subsequently, staging laparoscopy was performed during the 2nd term on patients who showed ring-enhanced lesions or nodular low-attenuation lesions (less than 10-mm diameter) of the liver on MD-CT. Seventy patients with pancreatic cancer who underwent pre-operative evaluation using SD-CT/angiography between January 2000 and August 2002 (1st term) served as the historical control group. During this period, staging laparoscopy was not performed. All operations were performed by two experienced hepato-pancreato-biliary surgeons who were in agreement about the extent of the surgery to be performed.

Settings for contrast-enhanced Multidetector row CT (MD-CT)

Since September 2002, MD-CT imaging on patients with pancreatic cancer has been performed using a Hi-speed advantage QX/I (General Electric Medical System, Milwaukee, WI). Arterial and portal phase images were collected using a 1.25 mm × 4-detector configuration and a multi-slice pitch of 3 (High quality mode), with a table speed of 3.75 mm/rotation. After reconstruction of the raw scans, data from serial 1.25-mm thick slices with a 0.6-mm interval were transferred to a workstation (Advantage Window 3.1). The scans were evaluated by an experienced hepatopancreatobiliary surgeon and a consultant radiologist. At the top of axial scans, 2D and 3D coronal and sagittal anatomical reconstructions were also performed. A recent publication from this unit6 provides more detailed information.

CT during hepatic arteriography (CTHA) and CT during arterioportgraphy (CTAP)

Between January 2000 and August 2002, patients with pancreatic cancer underwent CTHA/CTAP at the time of pre-operative angiography. As described previously (6), whole-liver scanning (single-slice helical CT: thickness 7 mm, interval 7 mm, 120 kV, 250 mA, 0.8 sec/rotation) was done for

CTAP and CTHA. CTHA/CTAP/angiography findings were evaluated independently by an experienced radiologist, and conventional SD-CT was performed with a slice thickness of 5 mm.

Comparison of pre-operative patient selection and grading of residual tumor with different pre-operative radiological modalities

Pre-operative patient selection and grading of residual tumors (R classification) were compared between 29 patients that underwent resection after pre-operative MDCT evaluation in the 2nd term, and 33 patients evaluated by SD-CT/angiography in the 1st term **(Table 1 and 2)**. Residual tumors were graded as follows: R0, radical resection with tumor-free resection margins; R1, palliative resection with microscopically proven tumor on resection margins; R2, palliative resection with macroscopically tumor-positive margins. For strict evaluation of surgical margins, intra-operative frozen or permanent pathological sections from the dissected stump of the extra-pancreatic nerve plexus around the celiac trunk or the superior mesenteric artery (SMA) and from retroperitoneal tissues were routinely used. All pathological findings were evaluated by an experienced pathologist according to the General Rules for Clinical and Pathological Management of Carcinoma of the Pancreas of the Japan Pancreas Society (9). Tumor staging was graded as M1 (stage IVb) when para-aortic lymph node metastasis was detected. There was one in-hospital death in each period.

Statistical analysis

All data are expressed as median values and range. Data analysis was undertaken using Statview Version 5.0 for Windows (Abacus Concepts, Inc. USA). When appropriate, chi-square or Fisher's exact tests were used for comparison of categorical variables. Kaplan-Meier curves of disease-free survival and overall survival were generated, and comparisons between the groups were performed using log-rank test.

RESULTS

Comparison of pre-operative patient selection and grading of residual tumor with different pre-operative radiological modalities.

Based on SD-CT/angiography images in the 1st term, 27 of 70 patients (39%) were classified as primary incurable or locally advanced cases. Among the 43 patients (61%) that were classified as potentially resectable, 10 patients (14%) underwent surgical exploration without pancreatic resection and 33 patients (47%) underwent resection **(Table 1)**. In the 2nd term, 80 patients were pre-operatively evaluated by MD-CT. Among 10 patients who displayed suspicious small metastases (less than 10-mm diameter) in the liver on MD-CT, subsequent staging laparoscopy confirmed the presence of liver metastases in seven, and the other three patients underwent pancreatectomy. In total, 48 of 80 patients (60%) in the 2nd term were not eligible for pancreatectomy, 29 patients (36%) underwent surgical resection and 4% underwent unnecessary laparotomy **(Table 1)**. Thus, introduction of MD-CT followed by staging laparoscopy in selected patients not only resulted in a higher frequency of primary diagnosed incurable or locally advanced cases, but also in fewer unresectable cases who underwent unnecessary laparotomy, relative to SD-CTs/angiography ($p<0.02$).

Table 2. Clinical Characteristics of Resected Cases in the 1st and 2nd Term

	1st term	2nd term	*p* factor
Total number of patients	*33*	*29*	n.s.
Age	64 (52-78)	65 (47 - 83)	n.s.
Gender(Male : Female)	17 : 16	13 : 16	n.s.
CA19-9 (U/ml)	93 (5-8470)	89 (1-9116)	n.s.
Site of primary lesion			
Head : Body-tail	24 : 9	23 : 6	n.s.
Tumor size (mm)	30 (13-90)	32 (16-80)	n.s.
Co-morbid disease (+:-)	16:17	16:13	n.s.
Pre-operative chemo-radiation (+:-)	8:25	20:9	p=0.0008
Type of surgery (PD:PpPD:TP:DP)	21:1:2:9	19:3:0:7	n.s.
PV resection (+:-)	8:25	5:24	n.s.
CA resection (+:-)	1:32	1:28	n.s.
Operative duration (min)	510(266-900)	565(265-815)	n.s.
Extent of blood loss (ml)	1390(450-5503)	1140(400-7250)	n.s.
Stage I:II:III:IVa:IVb	2:3:3:13:12	2:0:9:12:6	n.s.
Pathological differentiation (well:mod:por:other)	10:16:6:1	4:20:0:5	n.s.

The data was expressed as median (range). PD, pancreaticoduodenectomy; PpPD,pylorus preserving PD; TP,total pancreatectomy; DP,distal pancreatectomy; PV, portal vein; CA, Celiac trunk; mod,moderately; por,poorly; other, papillary/adenosquamous cell carcinoma.

There were few significant differences in the clinical backgrounds of the 29 patients in the 2nd term relative to the 33 patients in the 1st term **(Table 2)**. Patients in the 2nd term were significantly more likely to be treated pre-operatively with chemo-radiotherapy (p=0.0008). The frequency of portal vein resection, which was performed in 24% of 1st term and 21% of 2nd term patients, was not statistically different. In each term, distal pancreatectomy with celiac trunk resection was performed in one patient (3%). Of the cases that underwent pancreatectomy with vascular resection, 27% of tumors were R0 grade, 40% R1 and 33% R2. Although 25% of all R2-grade cases underwent this procedure, there was no significant difference in the frequency of R2 tumors resected in pancreatectomies with or without vascular resection.

In comparisons of residual tumor staging, the frequency of R0/1 in patients evaluated by MD-CT (80%) was significantly higher ($p<0.05$) than R0/1 evaluated by SD-CT/angiography (57%). The frequency of R2 grading was only 20% in the 2nd term, significantly less ($p<0.05$) than in the 1st term. All grade R1 cases showed microscopic tumor invasion to the retroperitoneal tissue or the stump of extra-pancreatic nerve plexus between the SMA and the pan-

creatic parenchyma. In contrast, R2 cases primarily showed major vessel invasions such as SMA, celiac trunk or common hepatic artery.

DISCUSSION

In this study, the pre-operative patient selection was compared to surgical resectability, and grading of residual tumor of patients with pancreatic cancer evaluated by MD-CT (slice thickness of 1.25 mm in the axial, coronal and sagittal phases) relative to conventional SD-CT/angiography (standard slice thickness of 5-7 mm). In selected patients, introduction of MD-CT followed by staging laparoscopy not only yielded a higher frequency of incurable or locally advanced cases during primary diagnosis, but also in fewer unresectable cases, relative to conventional forms of CT. Furthermore, the frequency of grade R0/1 tumors in patients evaluated by MD-CT was significantly higher than in patients evaluated by SD-CT/angiography. These data demonstrate that routine pre-operative imaging by MD-CT can significantly reduce the frequency of unnecessary surgical exploration and improve the selection of appropriate pancreatic cancer patients for surgical resection.

Technical developments in contrast enhanced MD-CT are useful not only for examination of thinner sections (which allow less partial-volume averaging to pick out mass lesions in solid organs, as well as different orthogonal plane display), but also for increased imaging speed (which allows greater bolus injection and a correspondingly higher concentration of iodine load to the portal vein and to the liver for better metastatic discernment). A faster injection rate also allows better segmentation of contrast phases. MD-CT cine-images with thin collimation in the axial, coronal and sagittal phases can provide detailed information in regions around peri-pancreatic major vessels and small liver metastases.

It is widely accepted that surgical resection is the only curative treatment that offers a significant chance for long-term survival in pancreatic cancer patients (10,11). Patients diagnosed with distal metastases, where the main treatment goal is to improve quality of life using less invasive procedures, should be managed non-surgically. Accurate staging to select patients who may benefit from resection is essential. Recent reports indicate that approximately one-third of patients diagnosed with resectable pancreatic tumors on CT were then found to have unresectable tumors upon surgery (12-15). This type of incorrect diagnosis is most often due to undetected vascular invasion, or small peritoneal or liver metastases. We reported previously that the accuracy of diagnosis of liver metastasis and vascular involvement by MD-CT in patients with pancreatic cancer was favorable compared to radiological findings from SD-CTs/angiography (6). Others have also reported that the sensitivity and specificity of vascular involvement diagnosis are 80-100% for MD-CT (16,17). These findings, and our experiences, lead us to conclude that accurate evaluation of liver metastasis and vascular involvement by MD-CT could result in fewer surgical cases without resection, and more curative cases relative to patients evaluated by SD-CT/angiography.

The problem of undetected metastases has led many surgeons to perform staging laparoscopy and laparoscopic biopsy routinely in an effort to avoid unnecessary laparotomy (12-14,18) . In this study, staging laparoscopy was performed in selected cases to confirm the presence of liver metastasis detected by MD-CT, because use of the operating room for pancreatic surgery was limited in our hospital. In cases where MD-CT detected a small liver mass (<10 mm in diameter, and not definitive for the diagnosis of liver metastasis), laparoscopic exploration, ultrasonography and biopsy were used for confirmation. The 4% frequency of unresectable cases found in the 2nd term of this study would be considered acceptable in usual clinical practice. Thus, we suggest that routine staging laparoscopy after MD-CT pre-operative evaluation is not essential for selecting resectable cases with reasonable accuracy.

Factors that define resectability include the sur-

Table 3. Resection Rates in Patients with Potentially Resectable Pancreatic Cancer Based on Different Imaging Modalities

	Imaging studies	n*	potentially resectable	resected	resection rate % (R0:1:2:%)	reason for unresected distant	local
Rumstadt *et al.*.27	CT	398	194	172	89 (NR)	NR	NR
White *et al.*.28	CT	103	68	38	56 (68:NR:NR)	18%	26%
Friess *et al.*.29	CT	119	102	71	70 (NR)	14%	16%
Saldinger *et al.*.30	CT	NR	52	36	69 (78: NR:NR)	6%	25%
Vollmer *et al.*.18	CT	84	84	47	56 (NR)	26%	17%
	Lap	84	60	47	78 (NR)	7%	13%
Jimenez *et al.*.12	Lap	125	31	23	74 (NR)	3%	23%
Ellsmere *et al.*.13	MD-CT	NR	44	23	52 (66:17:17)	18%	30%
Vargas *et al.*. 17	MD-CT	59	25	22	88 (95:5:0)	12%	0%
In this study							
2000-2002	CT	70	43	33	77(18:39:43)	18%	5%
2002-2005	MD-CT	80	32	29	91(52:28:20)	9%	0%

*Number of patients with pancreatic cancer. MD-CT, multidetector row-CT; NR, not reported; Lap, staging laparoscopy
Resection rate, resected number/potentially resectable number

geon's opinion on the necessity of venous or arterial resection (19-20), and whether high-risk margins for resection of a tumor are acceptable. In our center, pancreatectomy with portal vein or celiac trunk resection was performed in some cases in which resection had been predicted to generate surgical- or pathological-free margins. During the period of this study, surgical indication was fixed, and two experienced surgeons performed all resections. Relative to SD-CT/angiography, pre-operative evaluation using MD-CT led to a higher frequency of curative resection and fewer cases of palliative resection. The frequency of R0 resected cases in the 1st and 2nd term (18% and 52%, respectively) was relatively low; however in the 2nd term, the frequency of R0/R1 in resected cases was 80% (an acceptable value). Because we examined pathological specimens of the surgical stump of perineural and retroperitoneal fat tissues between the pancreatic parenchyma and the SMA or the CA strictly, the frequency of R1-grade resected cases was relatively high. All 1st- and 2nd-term R1-grade cases showed positive microscopic margins of perineural and retroperitoneal fat tissues, but no extended invasion into major peri-pancreatic arteries. The significant decrease observed in the frequency of R2-grade tumors in the 2nd term was attributed to cases involving extended invasion to the major peri-pancreatic artery. Thus, a use of MD-CT contributes to accurate pre-operative imaging of major peri-pancreatic vessel invasion. Relatively high rates of R2 operation at our facility may also be due to broad surgical indications. To reduce frequency of R2 resection, "potentially resectable" cases categorized in this study should be defined as tumor ingrowth with vessel contiguity less than 0-25%, but not less than 50% in the major peri-pancreatic artery.

A caveat to interpreting the increase in curative resection in the 2nd term as significant is that, in addition to surgical resection, there is a difference in the number of patients receiving pre-operative chemo-radiation therapy (CRT) between the 1st and 2nd terms. A group at Duke University has reported that pre-operative CRT, in particular, can result in down-staging of pancreatic cancers (21,22). Breslin *et al.* at the M. D. Anderson Cancer Center have suggested that patient survival time with potentially resectable pancreatic cancer is maximized by a combination of chemoradiation and pancreaticoduodenectomy (23). Authors of a recent review from Sweden suggested that neo-adjuvant therapy represents an interesting solution to the poor prognosis of pancreatic cancer, although trials that include random controls are lacking (24). In this study, the frequency of grade-R2 tumors in cases with CRT was similar to that in cases without CRT, and both univariate and multivariate analyses showed that CRT was not an independent factor for curative resection (data not shown). Overall, the effect of neo-adjuvant therapy on patients with pancreatic cancer is presently unclear and will require further study. In interpreting the results of this retrospective analysis, variables including type of operation, rate of portal vein and celiac trunk resection, operative time and extent of blood loss, showed no significant differences between the 1st term and the 2nd term (Table 2). However, we were unable to take other underlying variables, such as pre-operative chemoradiotherapy and an extended study period of approximately five years, into account.

Overall, nearly 80% of patients evaluated with staging laparoscopy underwent successful resection, relative to an average of 70% (range 56-89%) of patients evaluated with CE-CT (**Table 3**). Better detection of unsuspected distant metastases likely contributed to this increase in successful resection but is not likely to contribute significantly to any changes in the detection of locally advanced disease following staging laparoscopy. Clearly, laparoscopy can prevent unnecessary laparotomy in patients with CT-occult metastases that then appear as peritoneal or surface liver metastases (25,26). In the conventional CE-CT or staging laparoscopy cases, the most common cause of unresectability (around 20%) was the presence of locally advanced disease. These data question the value of laparoscopy in the detection of mesenteric or retroperitoneal vessel involvement. In contrast, thin-collimation MD-CT cine-images of axial, coronal and sagittal phases provide detailed information around peri-pancreatic major vessels. MD-CT data from this report, and from Vargas *et al.*, demonstrate that extended vascular invasion is not the most common cause of unresectability. Previously, Ellesmere *et al.* had reported that locally advanced disease was present in approximately 30% of cases evaluated with laparotomy, however, the MD-CT scanning parameters of their study included 5 mm-thick reconstruction slices, relative to the 0.6 mm-thick slices of our protocol.

In conclusion, the use of MD-CT, which allows extremely thin collimation and the acquisition of high-resolution images of the pancreas, has a significant impact on the prevention of unnecessary surgical exploration and the selection of appropriate pancreatic cancer patients for surgical resection.

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