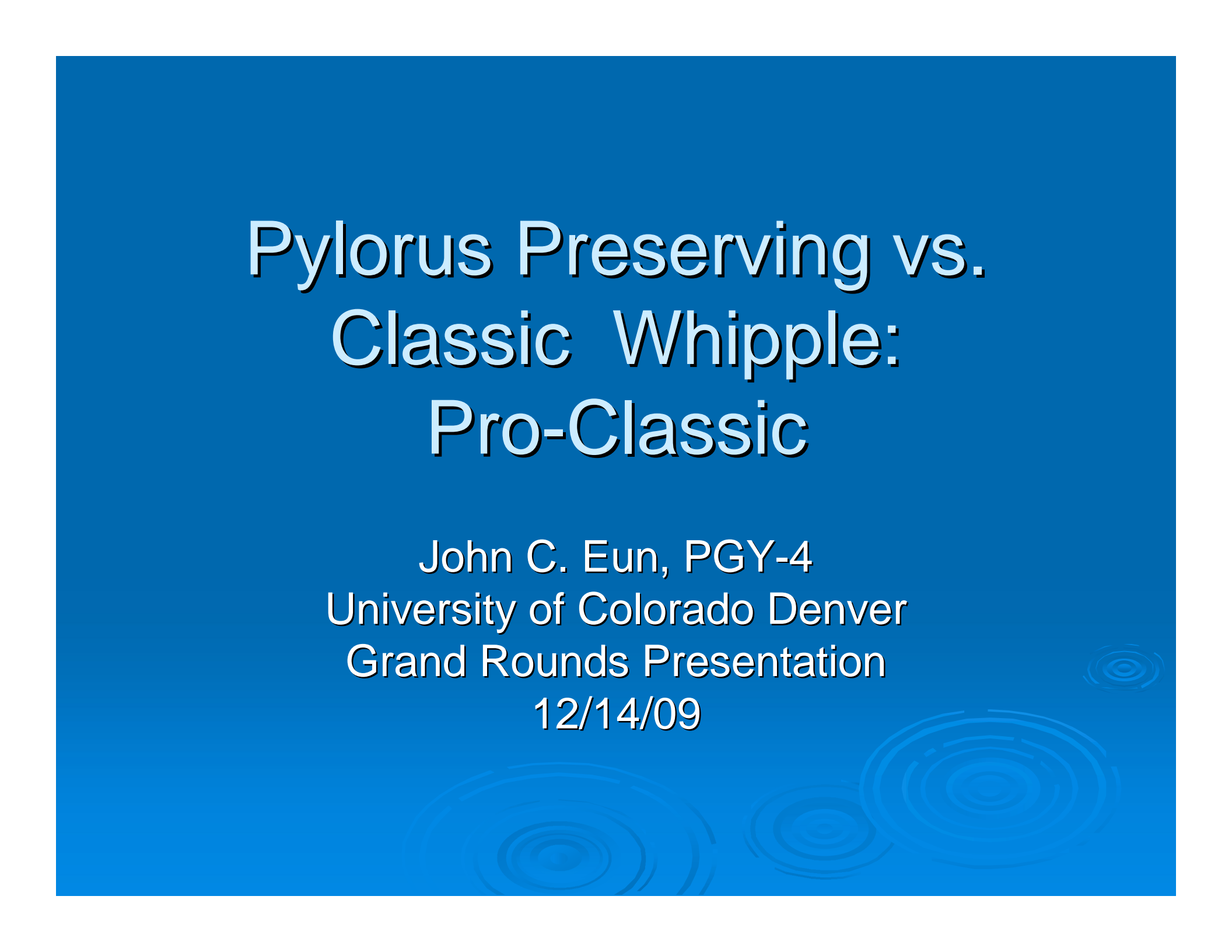


Pylorus Preserving vs. Classic Whipple: Pro-Classic

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University of Colorado Denver
Grand Rounds Presentation
12/14/09



Outline

- Background
- Description of Whipple
- Safety
- Benefits
- Treatment
- Conclusions

Incidence

Leading Sites of New Cancer Cases and Deaths – 2009 Estimates

| Estimated New Cases* | | Estimated Deaths | |
|--------------------------------------|--------------------------------------|---|--|
| Male | Female | Male | Female |
| Prostate 192,280 (25%) | Breast 192,370 (27%) | Lung & bronchus 88,900 (30%) | Lung & bronchus 70,490 (26%) |
| Lung & bronchus 116,090 (15%) | Lung & bronchus 103,350 (14%) | Prostate 27,360 (9%) | Breast 40,170 (15%) |
| Colon & rectum 75,590 (10%) | Colon & rectum 71,380 (10%) | Colon & rectum 25,240 (9%) | Colon & rectum 24,680 (9%) |
| Urinary bladder 52,810 (7%) | Uterine corpus 42,160 (6%) | Pancreas 18,030 (6%) | Pancreas 17,210 (6%) |
| Melanoma of the skin 39,080 (5%) | Non-Hodgkin lymphoma 29,990 (4%) | Leukemia 12,590 (4%) | Ovary 14,600 (5%) |
| Non-Hodgkin lymphoma 35,990 (5%) | Melanoma of the skin 29,640 (4%) | Liver & intrahepatic bile duct 12,090 (4%) | Non-Hodgkin lymphoma 9,670 (4%) |
| Kidney & renal pelvis 35,430 (5%) | Thyroid 27,200 (4%) | Esophagus 11,490 (4%) | Leukemia 9,280 (3%) |
| Leukemia 25,630 (3%) | Kidney & renal pelvis 22,330 (3%) | Urinary bladder 10,180 (3%) | Uterine corpus 7,780 (3%) |
| Oral cavity & pharynx 25,240 (3%) | Ovary 21,550 (3%) | Non-Hodgkin lymphoma 9,830 (3%) | Liver & intrahepatic bile duct 6,070 (2%) |
| Pancreas 21,050 (3%) | Pancreas 21,420 (3%) | Kidney & renal pelvis 8,160 (3%) | Brain & other nervous system 5,590 (2%) |
| All sites 766,130 (100%) | All sites 713,220 (100%) | All sites 292,540 (100%) | All sites 269,800 (100%) |

*Excludes basal and squamous cell skin cancers and in situ carcinoma except urinary bladder.

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Poor Prognosis

- The median survival for all stages of pancreatic cancer is less than 3-5 months from diagnosis
 - 5-year survival of 0.4-3%
- Although there have been some advances in chemotherapy (5-FU, gemcitabine), surgery still remains the only treatment
- After successful surgery the prognosis is still poor
 - Median survival: 13-15 months
 - 5-year survivals: 15- 20%

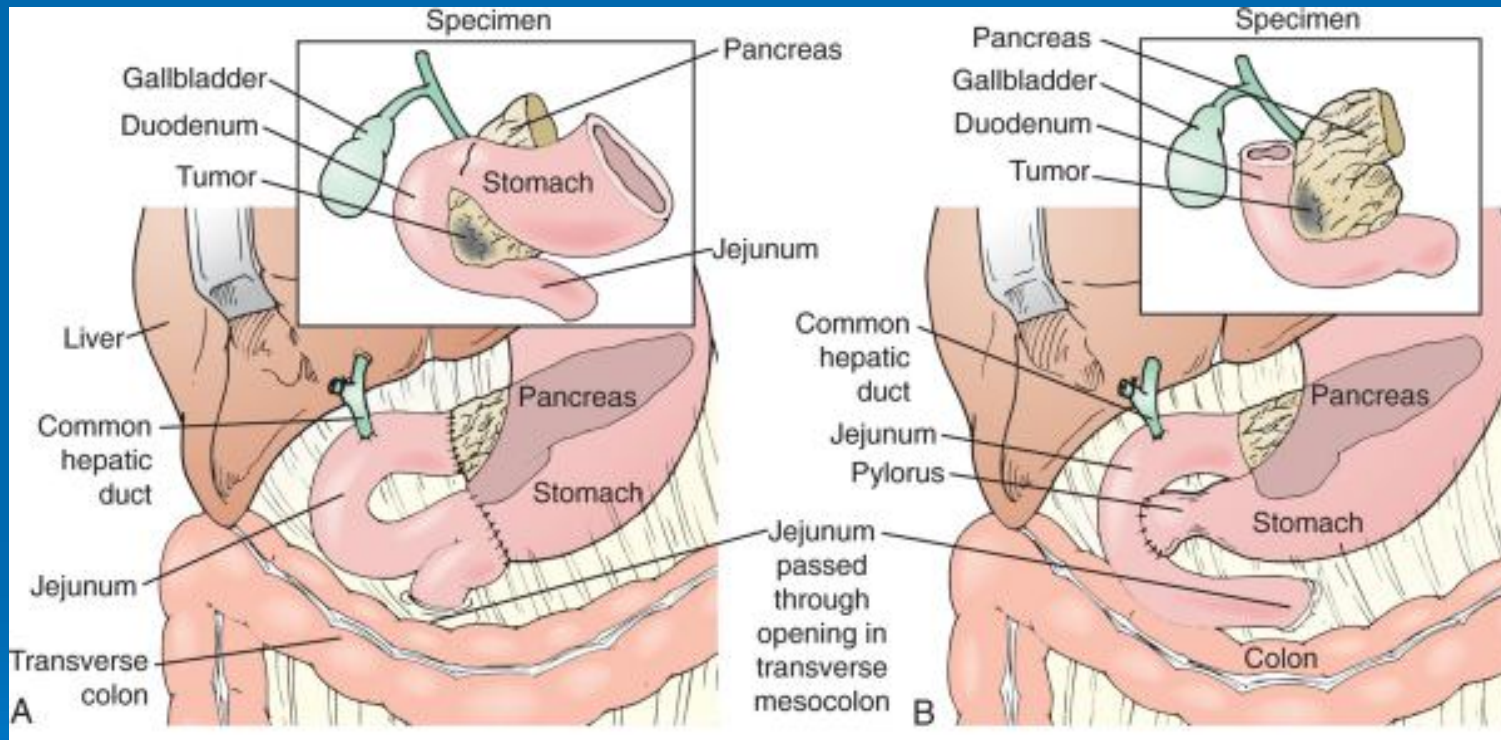
Two methods

- “Classic” Whipple: Pancreaticoduodenectomy
 - Developed by Walther Kausch in 1912
 - Modified by Allen Whipple 1935
 - en bloc resection:
 - Pancreatic head
 - Duodenum
 - Common bile duct
 - Gall Bladder
 - Distal portion of stomach
 - Adjacent lymph nodes

Two Methods

- “Pylorus-preserving” Whipple
 - Kenneth Watson 1942
 - Traverso and Longmire 1978
 - en bloc resection:
 - Pancreatic head
 - Duodenum
 - Common bile duct
 - Gall bladder
 - Preservation of the stomach and proximal 2-3 cm of the duodenum

Two Methods



Why Two?

➤ cWhipple

- Dumping
- Diarrhea
- Dyspepsia
- Weight loss

➤ ppWhipple

- Keep the stomach and (in theory) prevent the side effects
- Less radical operation
 - Less time?
 - Less recovery time?

BUT

- ppWhipple was initially described for periampullary tumors and chronic pancreatitis
- NOT treatment of cancer at the pancreatic head!
- Not be performed with patients with:
 - Bulky tumors of the pancreatic head
 - Duodenal tumors (1st, 2nd parts)
 - Lesions associated with grossly positive pyloric/peripyloric lymph nodes

So...

- Is the ppWhipple
 - Safe?
 - Benefits?
 - Treatment?



Safe?

- Early and late complications of pylorus-preserving pancreatoduodenectomy in Japan 1998.
- Yamaguchi K., et al.
- J Hepatobiliary Pancreat Surg 1999
- Retrospective study
- 74 Institutions
- 1066 patients with ppWhipple
- Analyzed early (within 1 month), and late (after 1 month) postoperative complications

Yamaguchi et al. 1999

| Early complications | # patients | # evaluated | Frequency (%) |
|------------------------------|-------------------|--------------------|----------------------|
| Delayed gastric emptying | 464 | 1016 | 46 |
| Pancreatojejunostomy leakage | 165 | 1041 | 16 |
| Intra-abdominal infection | 142 | 1055 | 14 |
| Cholangitis | 90 | 1014 | 8.9 |
| Hepaticojejunostomy leakage | 49 | 1041 | 4.7 |
| Intra-abdominal hemorrhage | 36 | 1036 | 3.5 |
| Upper GI hemorrhage | 33 | 1033 | 3.2 |
| Duodenojejunostomy leakage | 21 | 1027 | 2.0 |
| Operative mortality | 23 | 955 | 2.4 |

Yamaguchi et al. 1999

| Late complications | # patients | # evaluated | Frequency (%) |
|---------------------------|-------------------|--------------------|----------------------|
| Delayed gastric emptying | 215 | 913 | 24 |
| Stomal ulcer | 34 | 940 | 3.6 |
| Cholangitis | 64 | 962 | 6.7 |
| Liver abscess | 12 | 982 | 1.2 |

Safe?

Delayed gastric emptying is associated with pylorus-preserving but not classical Whipple pancreaticoduodenectomy: A review of the literature and critical reappraisal of the implicated pathomechanism

Kosmas I Paraskevas, Costas Avgerinos, Costas Manes, Dimitris Lytras, Christos Dervenis

World J Gastroenterol October 7, 2006 Volume 12 Number 37

- A literature review on cWhipple vs. ppWhipple in regards to DGE
- DGE Definition:
 - Inability to tolerate normal diet by 10-14 days post-op
 - Inability to tolerate liquid diet by POD #7
 - NGT in place for ≥ 10 days plus: emesis after NGT removal, reinsertion of NGT, use of prokinetic after post-op day 10, failure to progress with diet

Paraskevas, et al. 2006

Table 1 Association between DGE and PD/PPPD

| Study | Yr | Patients (n) | Results |
|---|------|--------------------------------------|---|
| Klinkenbijn <i>et al</i> ^[20] | 1992 | 91 (44 PDs, 47 PPPDs) | No difference with regards to DGE was demonstrated between the two groups (i.e. days to liquid and normal diet) |
| Roder <i>et al</i> ^[12] | 1992 | 110 (62 PDs, 48 PPPDs) | DGE was noted in 0 (0%) patients after PD and 9 (19%) patients after PPPD (<i>P</i> value not mentioned) |
| Patel <i>et al</i> ^[25] | 1995 | 67 (52 PDs, 15 PPPDs) | DGE was noted in 41% of the PD group and 61% of the PPPD group (<i>P</i> = 0.04) |
| Mosca <i>et al</i> ^[90] | 1997 | 218 (61 PDs, 157 PPPDs) | DGE was noted in 1 (4.7%) patient after PD and 14 (8.9%) patients after PPPD (<i>P</i> value not mentioned). |
| van Berge Henegouwen <i>et al</i> ^[34] | 1997 | 200 (100 PDs, 100 PPPDs) | DGE was noted in 34 patients after PD and 37 patients after PPPD (<i>P</i> = NS) ¹ |
| Lin and Lin ^[63] | 1999 | 30 (15 PDs, 15 PPPDs) | DGE was noted in 1 patient after PD and 6 patients after PPPD (<i>P</i> = 0.08, two-sided Fisher's exact test, NS) |
| Di Carlo <i>et al</i> ^[91] | 1999 | 113 (39 PDs, 74 PPPDs) | DGE was noted in 6 (15.3%) patients after PD and 9 (12.1%) patients after PPPD (<i>P</i> = NS) |
| Yeo <i>et al</i> ^[92] | 1999 | 106 (58 PDs, 48 PPPDs) ² | DGE was noted in 9 (16%) patients after PD and 2 (4%) patients after PPPD (<i>P</i> = 0.03) |
| Seiler <i>et al</i> ^[93] | 2000 | 77 (40 PDs, 37 PPPDs) | DGE was noted in 18 (45%) patients after PD and 12 (32%) patients after PPPD (<i>P</i> = 0.17, NS) |
| Martignoni <i>et al</i> ^[64] | 2000 | 62 (27 PDs, 35 PPPDs) | DGE was noted in 9 (33%) patients after PD and 13 (37%) patients after PPPD (<i>P</i> = NS) |
| Yamaguchi <i>et al</i> ^[94] | 2001 | 50 (27 PDs, 23 PPPDs) | DGE was significantly associated with PPPD compared with PD (gastric tube removal, <i>P</i> < 0.0001, oral intake, <i>P</i> = 0.0018) |
| Yeo <i>et al</i> ^[6] | 2002 | 294 (148 PDs, 146 PPPDs) | DGE was noted in 24 (16%) patients after PD and 9 (6%) patients after PPPD (<i>P</i> = 0.006) |
| Nguyen <i>et al</i> ^[95] | 2003 | 105 (50 PDs, 55 PPPDs) ³ | DGE was noted in 6 of 50 (12%) patients after PD and 4 of 55 (7%) patients after PPPD (<i>P</i> = 0.40, NS) |
| Horstmann <i>et al</i> ^[73] | 2004 | 132 (19 PDs, 113 PPPDs) ⁴ | DGE was noted in 4 of 19 (21%) patients after PD and 13 of 113 (12%) patients after PPPD (<i>P</i> = 0.11, NS) |
| Tran <i>et al</i> ^[77] | 2004 | 170 (83 PDs, 87 PPPDs) ⁵ | DGE was noted in 18 patients after PD and 19 patients after PPPD (<i>P</i> = 0.80, NS) |
| Seiler <i>et al</i> ^[96] | 2005 | 130 (66 PDs, 64 PPPDs) | DGE was noted in 30 (45%) patients after PD and 20 (31%) patients after PPPD (<i>P</i> = 0.096, NS) |
| Lin <i>et al</i> ^[97] | 2005 | 33 (19 PDs, 14 PPPDs) ⁶ | DGE was noted in 6 (43%) patients after PD and 0 patients after PPPD (<i>P</i> < 0.05) |

Benefits?

Pylorus Preserving Pancreaticoduodenectomy Versus Standard Whipple Procedure

*A Prospective, Randomized, Multicenter Analysis of 170 Patients
With Pancreatic and Periapillary Tumors*

Khe T. C. Tran, MD, Hans G. Smeenk, MD,* Casper H. J. van Eijck, MD, PhD,*
Geert Kazemier, MD,* Wim C. Hop, MSc, PhD,* Jan Willem G. Greve, MD, PhD,†
Onno T. Terpstra, MD, PhD,‡ Jan A. Zijlstra, MD,§ Piet Klinkert, MD,§ and Hans Jeekel, MD, PhD**

Annals of Surgery • Volume 240, Number 5, November 2004

- Multicenter, prospective RCT
- 170 pts with suspected pancreatic/periapillary tumor
- Randomized to cWhipple (83) or ppWhipple (87)

Tran, et al. 2004

| | cWhipple | ppWhipple | P-value |
|--------------------|-----------------|------------------|----------------|
| Intraop blood loss | 2L | 2L | 0.70 |
| Operative time | 300 minutes | 300 minutes | 0.10 |
| Intraop tranfusion | 2 units | 2 units | 0.70 |
| Hospital stay | 20 days | 18 days | 0.488 |

Benefits?

Randomized clinical trial of pylorus-preserving duodenopancreatectomy *versus* classical Whipple resection – long term results

C. A. Seiler, M. Wagner, T. Bachmann, C. A. Redaelli, B. Schmied, W. Uhl, H. Friess and M. W. Büchler

British Journal of Surgery 2005; 92: 547–556

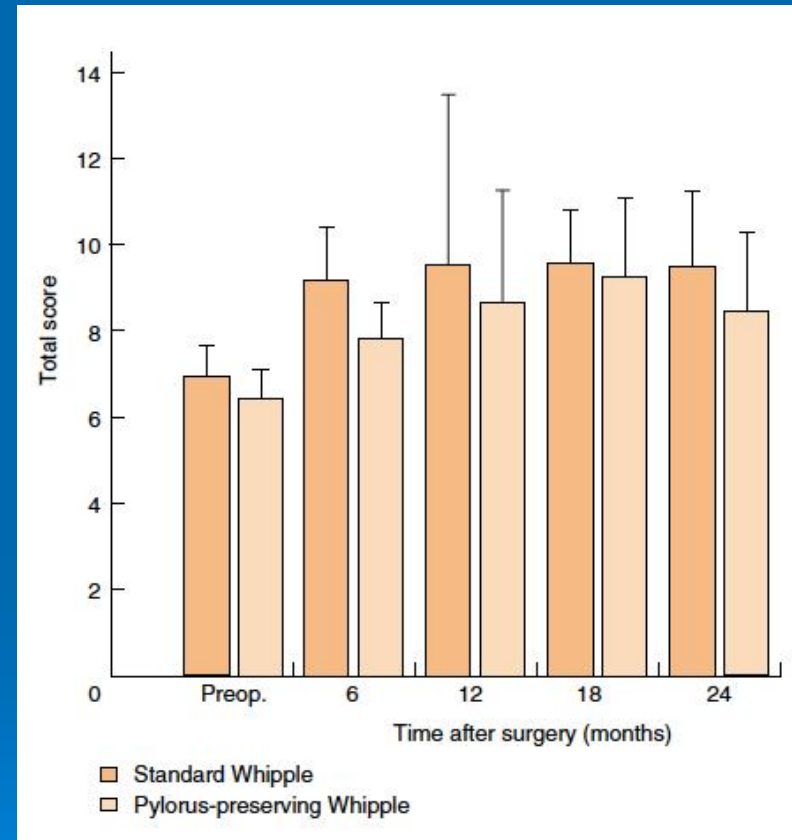
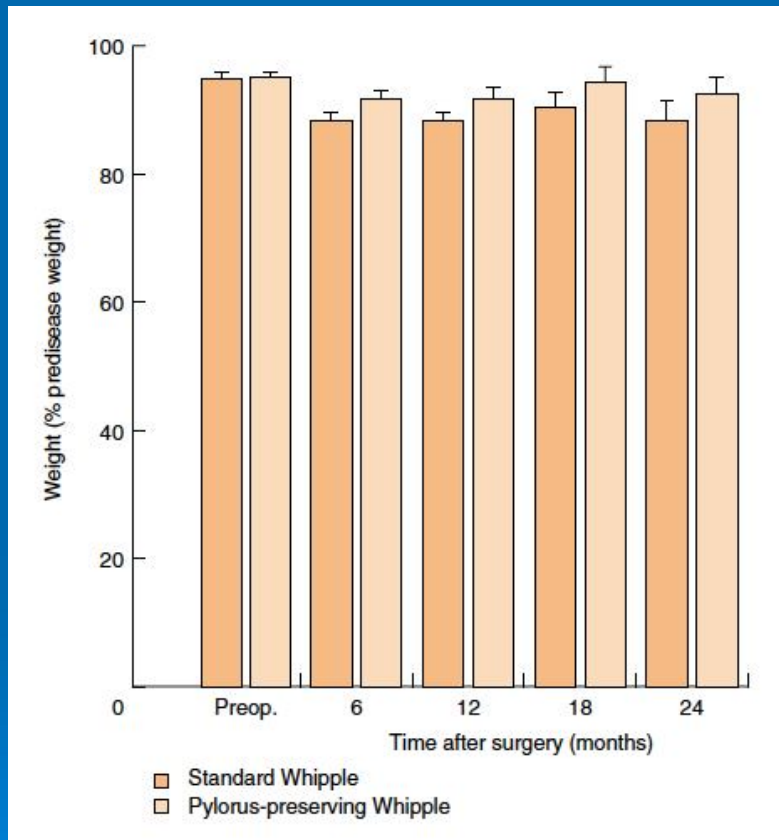
- 130 pts randomized to cWhipple or ppWhipple

Seiler, et al. 2005

Table 5 Surgical and medical morbidity, and mortality

| | Total (n = 130) | Standard Whipple (n = 66) | Pylorus-preserving Whipple (n = 64) | P |
|------------------------------|--------------------|------------------------------|---|--------|
| Surgical morbidity | | | | |
| Delayed gastric emptying* | 50 (38.5) | 30 (45) | 20 (31) | 0.096† |
| Bleeding | 6 (4.6) | 4 (6) | 2 (3) | 0.680‡ |
| Fistula | 3 (2.3) | 1 (2) | 2 (3) | 0.999‡ |
| Infection (wound or abscess) | 8 (6.2) | 4 (6) | 4 (6) | 0.999‡ |
| Medical morbidity | | | | |
| Pulmonary | 17 (13.1) | 10 (15) | 7 (11) | 0.435† |
| Cardiocirculatory | 8 (6.2) | 5 (8) | 3 (5) | 0.465‡ |
| Renal | 8 (6.2) | 3 (5) | 5 (8) | 0.489‡ |
| Other | 4 (3.1) | 1 (2) | 3 (5) | 0.361‡ |
| Relaparotomy | 3 (2.3) | 1 (2) | 2 (3) | 0.616‡ |
| Overall morbidity (%) | 80 (61.5) | 45 (68.2) | 35 (54.7) | 0.071† |
| Mortality | 3 (2.3) | 2 (3) | 1 (2) | 0.999‡ |

Seiler, et al. 2005



- No difference in weight gain

- No difference in quality of life

Treatment?

- Pancreatoduodenectomy with pyloric preservation for carcinoma of the pancreas: a cautionary note
- Sharp KW, et al. *Surgery* 1989
- Case study of 3 patients with cWhipple:
 - 2 w/ proximal, intramural, microscopic spread of pancreatic tumor within the duodenum/antrum

Sharp, et al.

- “The use of pylorus-sparing pancreatoduodenectomy in resectable pancreatic cancers must be viewed skeptically”

Treatment?

- Adequate lymphadenectomy
 - LN along the lesser gastric curvature and peri-pyloric region are not removed in the ppWhipple.

Treatment?

- Pylorus-preserving Whipple resection for pancreatic cancer. Is it any better?
- Patel A.G., et al. Arch Surg 1995
- Retrospective review of 67 pts who had a Whipple
- 52 cWhipple, 15 ppWhipple
- 5 LN in the ppWhipple group vs. 10 in the cWhipple group

Conclusions

- ppWhipple has serious complications
 - It is a radical surgery
- DGE-still controversy
- ppWhipple does not have the benefits to allow for a...
- Less adequate cancer operation

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