

Supplemental Data

Table S1 – Comparison between patients undergoing preoperative biliary drainage (group 1) and those not submitted to this procedure (group 2).

IQR: interquartile range; AST: aspartate aminotransferase; ALT: alanine aminotransferase; AP: alkaline phosphatase; GGT: gamma-glutamyl transferase; BR: bilirubin; CA 19.9: carbohydrate antigen 19.9; CEA: carcinoembryonic antigen; POPF: postoperative pancreatic fistula; CDC: Clavien-Dindo classification; AJCC: American Joint Committee on Cancer; DFS: disease free survival; OS: overall survival

| Variable | Preoperative biliary drainage | | <i>p</i> |
|----------------------|-------------------------------|-----------------------|----------|
| | Group 1: Yes (N=44) | Group 2: No (N=84) | |
| Age (years) | | | |
| Median (IQR) | 69 (61-74) | 69 (58.25-76) | 0.980 |
| Min-Max | 40-84 | 41-86 | |
| Gender | | | |
| Female (%) | 14 (31.8) | 36 (42.9) | 0.224 |
| Male (%) | 30 (68.2) | 48 (57.1) | |
| Preoperative sodium | | | |
| Median (IQR) | 137 (135.25-140) | 137 (134-139) | 0.369 |
| Min-Max | 129-142 | 128-144.7 | |
| Preoperative AST | | | |
| Median (IQR) | 52 (29-83) | 108 (45.50-199.50) | <0.001 |
| Min-Max | 17-252 | 9-668 | |
| Preoperative ALT | | | |
| Median (IQR) | 55 (28.50-110) | 140.50 (64.50-264.75) | <0.001 |
| Min-Max | 15-259 | 7-922 | |
| Preoperative FA | | | |
| Median (IQR) | 233 (124.50-343.50) | 434 (256-600.50) | <0.001 |
| Min-Max | 59-714 | 50-2100 | |
| Preoperative GGT | | | |
| Median (IQR) | 243 (70.50-401.25) | 450 (156-954) | 0.004 |
| Min-Max | 22-1362 | 10-3001 | |
| Preoperative BR | | | |
| Median (IQR) | 3.300 (1.600-10.675) | 15.85 (3.500-20.700) | 0.001 |
| Min-Max | 0.3-29.2 | 0.3-31.7 | |
| Preoperative Albumin | | | |
| Median (IQR) | 3.600 (3.200-3.850) | 3.700 (3.100-4.000) | 0.461 |
| Min-Max | 2.3-7.3 | 1.7-41.0 | |

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|------------------------------------|--------------------|----------------------|-------|
| Preoperative CA 19.9 | | | |
| Median (IQR) | 163 (32-949) | 243.5 (36.25-978.75) | 0.902 |
| Min-Max | 2-23911 | 2-6879 | |
| Preoperative CEA | | | |
| Median (IQR) | 3.25 (1.925-6.700) | 3.2 (1.9-4.9) | 0.538 |
| Min-Max | 0.6-105 | 0.6-49 | |
| Postoperative hospital stay (days) | | | |
| Median (IQR) | 13 (10-16) | 13 (9-20) | 0.763 |
| Min-Max | 6-36 | 3-85 | |
| NSQIP- Surgical Risk Calculator | | | |
| Any complications | | | |
| Mean (Min-Max) | 30.474 (19-42.4) | 28.982 (17-36.2) | 0.305 |
| Surgical site infection | | | |
| Mean (Min-Max) | 18.858 (13.3-24.6) | 17.769 (12.8-21) | 0.123 |
| Readmission | | | |
| Mean (Min-Max) | 16.142 (11.4-20.8) | 15.331 (8.2-20) | 0.295 |
| Reintervention | | | |
| Median (IQR) | 5.2 (4.3-6.1) | 4.9 (4.3-5.4) | 0.383 |
| Min-Max | 4.1-6.6 | 3.1-7.3 | |
| Death | | | |
| Median(IQR) | 0.8 (0.4-1.7) | 0.6 (0.2-1.5) | 0.440 |
| Min-Max | 0.1-6.5 | 0-3.4 | |
| Sepsis | | | |
| Mean (Min-Max) | 8.379 (4.7-12.2) | 7.992 (3-13.1) | 0.533 |
| Delayed gastric emptying | | | |
| Mean (Min-Max) | 15.389 (6.4-25.4) | 15.979 (9.3-25.3) | 0.610 |
| Operative time (hours) | | | |
| Median (IQR)) | 7 (6-8.5) | 7.75 (6.375-9) | 0.212 |
| Min-Max | 4-16.5 | 3-11 | |
| Postoperative morbidity | | | |
| Yes (%) | 36 (81.8) | 60 (71.4) | 0.277 |
| No (%) | 8 (18.2) | 22 (26.2) | |
| Postoperative hemorrhage | | | |
| Yes (%) | 7 (15.9) | 9 (10.7) | 0.428 |
| No (%) | 37 (84.1) | 73 (86.9) | |
| Intraabdominal abscess | | | |
| Yes (%) | 6 (13.6) | 18 (21.4) | 0.257 |
| No (%) | 38 (86.4) | 64 (76.2) | |
| Surgical site infection | | | |
| Yes (%) | 3 (6.8) | 9 (10.7) | 0.539 |
| No (%) | 41 (93.2) | 73 (86.9) | |
| POPF grade B or C | | | |

| | | | |
|---------------------------------------|----------------|---------------|--------|
| Yes (%) | 7 (16.7) | 12 (15.6) | 0.878 |
| No (%) | 35 (83.3) | 65 (84.4) | |
| Delayed gastric emptying grade B or C | | | |
| Yes (%) | 13 (29.5) | 25 (29.8) | 0.976 |
| No (%) | 30 (68.2) | 57 (67.9) | |
| Readmission | | | |
| Yes (%) | 22 (50) | 41 (48.8) | 1.000 |
| No (%) | 22 (50) | 41 (48.8) | |
| CDC ≥ III | | | |
| Yes (%) | 13 (29.5) | 26 (31) | 0.802 |
| No (%) | 31 (70.5) | 56 (66.7) | |
| Postoperative mortality | | | |
| Yes (%) | 2 (4.5) | 9 (11) | 0.223 |
| No (%) | 49 (95.5) | 73 (89) | |
| Intraoperative bile culture | | | |
| Positive (%) | 20 (45.5) | 3 (3.6) | <0.001 |
| Negative (%) | 12 (27.3) | 45 (55.3) | |
| Multidrug-resistant bacteria | | | |
| Yes (%) | 9 (45) | 1 (33.3) | 1.000 |
| No (%) | 11 (55) | 2 (66.7) | |
| Perioperative blood transfusion | | | |
| Yes (%) | 21 (47.7) | 24 (28.6) | 0.031 |
| No (%) | 23 (52.3) | 60 (71.4) | |
| AJCC pT | | | |
| pT1-T2 (%) | 36 (81.8) | 67 (79.8) | 0.780 |
| pT3-T4 (%) | 8 (18.2) | 17 (20.2) | |
| Size (cm) | | | |
| Median (IQR) | 2.55 (2.4-3.5) | 3.2 (2.675-4) | 0.036 |
| Min-Max | 1.5-9 | 0.4-6.5 | |
| AJCC pN | | | |
| N0 (%) | 8 (18.2) | 20 (23.8) | 0.464 |
| N1-N2 (%) | 36 (81.8) | 64 (76.2) | |
| AJCC stage | | | |
| I-II (%) | 30 (68.2) | 62 (73.8) | 0.501 |
| III-IV (%) | 14 (31.8) | 22 (26.2) | |
| Margins | | | |
| R0 (%) | 22 (50) | 39 (46.4) | 0.701 |
| R1-R2 (%) | 22 (50) | 45 (53.6) | |
| Lymphovascular invasion | | | |
| Yes (%) | 40 (90.9) | 63 (75) | 0.031 |
| No (%) | 4 (9.1) | 21 (25) | |
| Perineural invasion | | | |

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|-----------------------|------------|------------|-------|
| Yes (%) | 42 (95.5) | 74 (88.1) | 0.217 |
| No (%) | 2 (4.5) | 10 (11.9) | |
| Recurrence | | | 0.453 |
| Yes (%) | 26 (66.7) | 44 (59.5) | |
| No (%) | 13 (33.3) | 30 (40.5) | |
| Local recurrence | | | 0.297 |
| Yes (%) | 13 (50) | 16 (36.4) | |
| No (%) | 13 (50) | 27 (61.4) | |
| Pulmonary recurrence | | | 0.048 |
| Yes (%) | 15 (57.7) | 14 (31.8) | |
| No (%) | 11 (42.3) | 28 (63.6) | |
| Hepatic recurrence | | | 0.587 |
| Yes (%) | 15 (57.7) | 27 (61.4) | |
| No (%) | 11 (42.3) | 15 (34.1) | |
| Peritoneal recurrence | | | 0.828 |
| Yes (%) | 5 (19.2) | 9 (20.5) | |
| No (%) | 21 (80.8) | 33 (75) | |
| DFS (months) | | | 0.192 |
| Median (Min-Max) | 10 (3-61) | 8 (0-25) | |
| 3-year DFS (%) | 7.7 | 0 | |
| 5-year DFS (%) | 3.8 | 0 | |
| OS (months) | | | 0.833 |
| Median (Min-Max) | 20 (0-120) | 18 (0-156) | |
| 3-year OS (%) | 30.2 | 27.8 | |
| 5-year OS (%) | 18.1 | 18.5 | |

Table S2 – Comparison between patients undergoing preoperative biliary drainage by endoscopic retrograde cholangiopancreatography (ERCP) (group 1.1) and by percutaneous transhepatic cholangiography (PTC) (group 1.2).

IQR: interquartile range; AST: aspartate aminotransferase; ALT: alanine aminotransferase; AP: alkaline phosphatase; GGT: gamma-glutamyl transferase; BR: bilirubin; CA 19.9: carbohydrate antigen 19.9; CEA: carcinoembryonic antigen; POPF: postoperative pancreatic fistula; CDC: Clavien-Dindo classification; AJCC: American Joint Committee on Cancer; DFS: disease free survival; OS: overall survival

| Variable | Preoperative biliary drainage - route | | <i>p</i> |
|-------------------------------------------------|---------------------------------------|--------------------------------|----------|
| | Group 1.1: ERCP (N=27) | Group 1.2: CPT (N=17) | |
| Age (years) Mean (Min-Max) | 65.04 (40-83) | 71.47 (59-84) | 0.034 |
| Gender | | | |
| Female (%) | 8 (29.6) | 6 (35.3) | 0.694 |
| Male (%) | 19 (70.4) | 11 (64.7) | |
| Preoperative sodium Mean (Min-Max) | 138.222 (132-142) | 135.588 (129-142) | 0.01 |
| Preoperative AST Median (IQR) Min-Max | 46 (27-72) 19-174 | 60.50 (38.75-108.50) 17-252 | 0.253 |
| Preoperative ALT Median (IQR) Min-Max | 54 (26-111) 16-259 | 56 (38.50-117) 15-158 | 0.847 |
| Preoperative FA Median (IQR) Min-Max | 203 (118-396) 59-714 | 235 (149-303) 59-458 | 0.819 |
| Preoperative GGT Median (IQR) Min-Max | 237 (47-445) 23-1362 | 313 (145-369) 22-1200 | 0.971 |
| Preoperative BR Median (IQR) Min-Max | 3 (1.5-4.5) 0.3-29.2 | 9 (1.85-11.90) 1.3-22.9 | 0.162 |
| Preoperative Albumin Median (IQR) Min-Max | 3.7 (3.325-3.950) 2.3-4.4 | 3.4 (3.1-3.850) 2.3-7.3 | 0.482 |
| Preoperative CA 19.9 Median (IQR) Min-Max | 216 (53.0675-571.25) 2.27-2429 | 163 (3.7-2144) 2-23911 | 0.751 |
| Preoperative CEA | | | |

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|------------------------------------|--------------------|--------------------|-------|
| Median (IQR) | 3.3 (1.95-5.35) | 3.1 (1.5-8.8) | 0.885 |
| Min-Max | 0.67-20 | 0.6-3.1 | |
| Drainage time (days) | | | |
| Median (IQR) | 33 (23-63.50) | 22 (15-38) | 0.027 |
| Min-Max | 6-507 | 7-108 | |
| Drainage-related morbidity | | | |
| Yes (%) | 10 (37) | 11 (64.7) | 0.074 |
| No (%) | 17 (63) | 6 (35.3) | |
| Drainage-related morbidity | | | |
| Acute cholangitis | | | |
| Yes (%) | 6 (60) | 2 (18.2) | 0.080 |
| No (%) | 4 (40) | 8 (81.8) | |
| Acute pancreatitis | | | |
| Yes (%) | 3 (30) | 0 | 0.090 |
| No (%) | 7 (70) | 11 (100) | |
| Bleeding | | | |
| Yes (%) | 0 | 3 (27.3) | 0.214 |
| No (%) | 10 (100) | 8 (72.7) | |
| Obstruction | | | |
| Yes (%) | 2 (20) | 0 | 0.214 |
| No (%) | 8 (80) | 11 (100) | |
| Drain mobilization | | | |
| Yes (%) | 0 | 6 (54.5) | 0.012 |
| No (%) | 10 (100) | 5 (45.5) | |
| Postoperative hospital stay (days) | | | |
| Median (IQR) | 13 (10-21) | 11 (8-29) | 0.068 |
| Min-Max | 6-36 | 8-29 | |
| NSQIP- Surgical Risk Calculator | | | |
| Any complications | | | |
| Mean (Min-Max) | 28.167 (19-37.5) | 34.429 (29.1-42.4) | 0.020 |
| Surgical site infection | | | |
| Mean (Min-Max) | 18.575 (13.3-24.6) | 19.343 (14.8-21.7) | 0.610 |
| Readmission | | | |
| Mean (Min-Max) | 15.133 (11.4-19.5) | 17.871 (15.4-20.8) | 0.020 |
| Reintervention | | | |
| Median (IQR) | 4.5 (4.225-5.425) | 5.8 (5.4-6.2) | 0.034 |
| Min-Max | 4.1-6.2 | 4.6-6.6 | |
| Death | | | |
| Median (IQR) | 0.4 (0.125-1.375) | 1.9 (0.9-3.6) | 0.005 |
| Min-Max | 0.1-1.7 | 0.8-6.5 | |
| Sepsis | | | |

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|-------------------------------------------------------------|------------------------|-----------------------|-------|
| Mean (Min-Max) Delayed gastric emptying | 7.517 (4.7-11.5) | 9.857 (7.7-12.2) | 0.025 |
| Mean (Min-Max) | 15.067 (6.4-25.4) | 15.943 (12.6-21.5) | 0.695 |
| Operative time (hours) Median (IQR)) Min-Max | 7 (6-8.375) 4-16.5 | 8 (6-9) 4-11 | 0.531 |
| Postoperative morbidity Yes (%) No (%) | 24 (88.9) 3 (11.1) | 12 (70.6) 5 (29.4) | 0.227 |
| Postoperative hemorrhage Yes (%) No (%) | 5 (18.5) 22 (81.5) | 2 (11.8) 15 (88.2) | 0.689 |
| Intraabdominal abscess Yes (%) No (%) | 6 (22.2) 21 (77.8) | 0 17 (100) | 0.067 |
| Surgical site infection Yes (%) No (%) | 3 (11.1) 24 (88.9) | 0 17 (100) | 0.272 |
| POPF grade B or C Yes (%) No (%) | 5 (20) 20 (80) | 2 (11.8) 15 (88.2) | 0.482 |
| Delayed gastric emptying grade B or C Yes (%) No (%) | 12 (44.4) 15 (55.6) | 1 (5.9) 15 (88.2) | 0.014 |
| Readmission Yes (%) No (%) | 14 (51.9) 13 (48.1) | 8 (47.1) 9 (52.9) | 0.757 |
| CDC ≥ III Yes (%) No (%) | 16 (59.3) 11 (40.7) | 15 (88.2) 2 (11.8) | 0.040 |
| Postoperative mortality Yes (%) No (%) | 1 (3.7) 26 (96.3) | 1 (5.9) 16 (94.1) | 1.000 |
| Intraoperative bile culture Positive (%) Negative (%) | 15 (55.6) 5 (18.5) | 5 (29.4) 7 (41.2) | 0.130 |
| Multidrug-resistant bacteria Yes (%) No (%) | 7 (46.7) 8 (53.3) | 2 (40) 3 (60) | 1.000 |
| Perioperative blood transfusion Yes (%) | 13 (48.1) | 8 (47.1) | 0.944 |

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|-------------------------|---------------|---------------|-------|
| No (%) | 14 (51.9) | 9 (52.9) | |
| AJCC pT | | | |
| pT1-T2 (%) | 20 (74.1) | 16 (94.1) | 0.125 |
| pT3-T4 (%) | 7 (25.9) | 1 (5.9) | |
| Size (cm) | | | |
| Median (IQR) | 3 (2.45-3.65) | 2.5 (2.3-3.5) | 0.307 |
| Min-Max | 1.5-9 | 1.8-4.5 | |
| AJCC pN | | | |
| N0 (%) | 4 (14.8) | 4 (23.5) | 0.690 |
| N1-N2 (%) | 23 (85.2) | 13 (76.5) | |
| AJCC stage | | | |
| I-II (%) | 17 (63) | 13 (76.5) | 0.349 |
| III-IV (%) | 10 (37) | 4 (23.5) | |
| Margins | | | |
| R0 (%) | 13 (48.1) | 9 (52.9) | 0.757 |
| R1-R2 (%) | 14 (51.9) | 8 (47.1) | |
| Lymphovascular invasion | | | |
| Yes (%) | 24 (88.9) | 16 (94.1) | 1.000 |
| No (%) | 3 (11.1) | 1 (5.9) | |
| Perineural invasion | | | |
| Yes (%) | 25 (92.6) | 17 (100) | 0.515 |
| No (%) | 2 (7.4) | 0 | |
| Recurrence | | | |
| Yes (%) | 16 (66.7) | 10 (66.7) | 1.000 |
| No (%) | 8 (33.3) | 5 (33.3) | |
| Local recurrence | | | |
| Yes (%) | 8 (50) | 5 (50) | 1.000 |
| No (%) | 8 (50) | 5 (50) | |
| Pulmonary recurrence | | | |
| Yes (%) | 11 (68.8) | 4 (40) | 0.228 |
| No (%) | 5 (31.3) | 6 (60) | |
| Hepatic recurrence | | | |
| Yes (%) | 7 (43.8) | 8 (80) | 0.109 |
| No (%) | 9 (56.3) | 2 (20) | |
| Peritoneal recurrence | | | |
| Yes (%) | 2 (12.5) | 3 (30) | 0.340 |
| No (%) | 14 (87.5) | 7 (70) | |
| DFS (months) | | | |
| Median (Min-Max) | 10 (5-61) | 5 (3-19) | 0.017 |
| 3-year DFS (%) | 12.5 | 0 | |
| 5-year DFS (%) | 6.3 | 0 | |
| OS (months) | | | |
| Median (Min-Max) | 24 (0-120) | 14 (0-92) | 0.258 |

| | | | |
|---------------|------|------|--|
| 3-year OS (%) | 36.5 | 18.5 | |
| 5-year OS (%) | 18.2 | 18.5 | |