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# Upfront Surgery and Surgery Following Neoadjuvant Treatment of Pancreatic Ductal Adenocarcinoma: A Comparative Analysis of Short-term Postoperative Outcomes

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**Abstract.** *Background/Aim: In cases where neoadjuvant treatment (NAT) is administered, research on short-term postoperative outcomes appears to be insufficient. We compared short-term outcomes of upfront surgery (UpS) cases and NAT cases for pancreatic ductal adenocarcinoma (PDAC). Patients and Methods: We retrospectively reviewed 1,228 cases that had elective pancreatectomy at Samsung Medical Center from 2010 to 2020. All cases were classified into resectable pancreatic cancer (RPC) and locally advanced pancreatic cancer (LAPC) according to NCCN guidelines 2017. In each group, factors were compared between the UpS and NAT groups. Results: Rate of vascular resection was higher in the NAT group in RPC, compared to that in the NAT group in LAPC. Short-term postoperative outcomes had no significant differences between the UpS and NAT groups in both RPC and LAPC. Conclusion: In the NAT group, there were no significant differences from UpS in terms of short-term postoperative outcomes. Conversion surgery following NAT is a favorable strategy.*

Although recent studies show that the 5-year survival rates of pancreatic cancer have improved, they are still lower compared with other cancers (1, 2). In order to overcome poor outcomes, multidisciplinary evaluation and management have been performed together including surgery, oncology, radiation, radiological imaging, intervention, endoscopy, and pathology (3, 4). Among these, radical resection of the primary cancer with lymphadenectomy is necessary (3, 5-7). Improvement in long-term and short-term postoperative outcomes achieved by radical resection has been reported in numerous studies for a long time (8-13). In addition, the concept of pancreatic cancer as a systemic disease has been widely accepted. Therefore, systemic therapy along with surgical resection have become important in order to improve outcomes (14-16). Thus, upfront surgery followed by adjuvant systemic therapy has become the standard approach to pancreatic cancer treatment and improved outcomes have also been reported in many studies (5, 17-20). Despite significant improvement in long-term outcomes including overall survival, this strategy of postoperative adjuvant therapy has been challenged, because the planned schedule of adjuvant therapy can be disrupted due to complications occurring after surgery. Furthermore, the neoadjuvant setting before surgery can help identify whether the tumor is biologically unfavorable and progress rapidly despite resection (5, 19, 21, 22). Above all, it is important that the neoadjuvant treatment (NAT) is helpful by increasing the likelihood and radicality of resection *via* downstaging of the tumor. Previous studies have shown that NAT offers substantial benefit in outcomes including survival for borderline resectable and unresectable pancreatic cancer (23-27). There have also been studies showing that NAT was effective for resectable pancreatic cancer as well (28-31).

The administration of systemic therapy before surgery has been sufficiently proposed as an alternative to postoperative adjuvant therapy, and has been increasingly performed. However, most studies that reported the effectiveness of NAT to date have analysed the long-term postoperative outcomes. The research on short-term postoperative outcomes appears to be insufficient. Therefore, we aimed to compare the short-term postoperative outcomes of patients who underwent upfront surgery and those who underwent neoadjuvant treatment followed by surgery for pancreatic ductal adenocarcinoma (PDAC) in our high-volume single center.

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*Key Words:* Resectable pancreatic cancer, locally advanced pancreatic cancer, upfront surgery, neoadjuvant treatment, short-term postoperative outcomes.

## Patients and Methods

*Patients and data collection*. We collected data of consecutive patients diagnosed with PDAC who underwent elective pancreatectomy including pylorus preserving pancreaticoduodenectomy (PPPD), pylorus resecting pancreaticoduodenectomy (PRPD), distal pancreatectomy (DP), and total pancreatectomy (TP) at Samsung Medical Center in Seoul, South Korea, from January 2010 to March 2020. In our center, the frequency of NAT has increased gradually since 2010, therefore the starting point of inclusion in this study was set to 2010. All cases of pancreatectomy performed with curative intent were included and cases with distant metastasis confirmed in preoperative evaluation were excluded. A total of 1,228 cases were included and analysed. Data were collected from electronic medical records of our center and reviewed retrospectively. This study was approved by the Institutional review board (IRB) of Samsung Medical Center to search the data of included patients (IRB number: 2020-09-092). Our IRB waived the need for written informed consent from patients because this study was retrospectively designed.

We reviewed the preoperative imaging examinations such as CT or MRI of all the patients to identify whether the major blood vessel was in contact with the tumor, and if so, the angle of contact. We determined resectability according to the National Comprehensive Cancer Network (NCCN) guidelines version 2017 (20). All cases were classified into three groups of resectable, borderline resectable, and unresectable pancreatic cancer. Borderline resectable and unresectable pancreatic cancer were collectively referred to as locally advanced pancreatic cancer. Thus, all the cases in this study were divided into the resectable pancreatic cancer (RPC) group and the locally advanced pancreatic cancer (LAPC) group.

Each of the RPC and the LAPC groups was divided further into two groups of upfront surgery (UpS group) and neoadjuvant treatment followed by surgery (NAT group). Many preoperative factors and postoperative factors including various complications were compared between the groups RPC and LAPC. The discrepancy in the number of patients between the UpS group and the NAT group was too large, therefore we conducted propensity score matching (PSM) analysis to extract balanced cases. For matching factors, several preoperative factors such as age, gender, body mass index (BMI), American society of anesthesiologist (ASA) score, diabetes mellitus (DM), and initial tumor size were used.

We thoroughly reviewed the electronic medical records to find whether major blood vessels invaded by the tumor were resected and whether other organs were resected together, which was distinct from vascular resection.

In order to analyze the pathological characteristics of each group, various information including stage was obtained. We commonly reset the stage of entire cohort according to the 8th American Joint Committee Cancer (AJCC) Staging System. T stage is determined only by the tumor size (32). Regarding resection margin, R0 indicates both grossly and microscopically margin-negative resection and R2 indicates the presence of residual tumor even grossly. The case of resected margin microscopically found within 1mm from the tumor is determined as R1 (33, 34).

In the short-term postoperative outcomes, the keyword of our study, the short-term refers to within 90 days after surgery. We investigated length of stay (hospitalization days), general complications, postoperative pancreatic fistula (POPF), unplanned readmission, and mortality. Readmission and mortality within 30 days after surgery were also searched. General complications were graded according to the Clavien-Dindo classification (35). Grades I and II were referred to as minor complications, and from IIIa, they were referred to as major complications that required special managements such as intervention, surgery, intensive care, and others (36). The POPF, a specific complication after pancreatectomy, was graded based on the criteria of the International Study Group of Pancreatic Surgery (ISGPS) updated in 2016 (37). POPF grades B and C were collectively referred to as clinically relevant POPF (CR-POPF), which required further management that differed from the expected postoperative pathway (38, 39).

*Statistical analysis*. All statistical analyses comparing clinical, operative, pathological characteristics, and short-term postoperative outcomes were conducted using the IBM SPSS statistical software, version 27 (Chicago, IL, USA). Continuous variables between the groups were compared using the independent *t*-test, and categorical data were analyzed with the chi-square test. Differences with a probability (*p*) value of 0.05 or less were considered statistically significant. As mentioned previously, we conducted PSM in order to balance the UpS group and the NAT group using several preoperative factors. We used the R statistical software version 4.0.0 to execute the PSM, and used the nearest neighbor matching method with caliper width 0.25 of the standard deviation of the logit of propensity score. To extract the PSM dataset, six variables including age, gender, BMI, DM, ASA score, and initial tumor size were applied.

## Results

*Clinical, operative, and pathological characteristics*. Figure 1 shows the number of patients in each group. The entire cohort of 1,228 patients included 879 cases in the RPC group and 349 cases in the LAPC group. The most common cause of classification into the LAPC group was the greater than 180˚ contact between tumor and portal vein (PV) or superior mesenteric vein (SMV). The next highest proportion was the case of celiac axis or common hepatic artery invasion. In addition, there were cases of superior mesenteric artery (SMA)/SMV jejunal branch invasion, SMA invasion, inferior vena cava (IVC) invasion, and others. The UpS group and the NAT group included 859 and 20 patients in the RPC group, and 277 and 72 patients in the LAPC group, respectively. As a result of conducting PSM analysis, the balancing accuracy was the highest when matched in the ratio of 1:3 and 1:1, respectively. After PSM, 60 *versus* 20 patients in RPC and 68 *versus* 68 patients in LAPC were balanced in the UpS group and the NAT group, respectively.

The clinical, operative, and pathological characteristics and the short-term postoperative outcomes of each group before PSM are shown in Table I. In LAPC, patients in the UpS group were significantly older (63.4 years *versus* 60.1 years) and had significantly lower body weight (59.9 kg *versus* 62.7 kg) than those in the NAT group. The distribution of underlying DM patients in RPC was found to be significantly less in the UpS group (38.3%) and greater (65.0%) in the NAT group. In LAPC, the initial tumor size was significantly larger in the

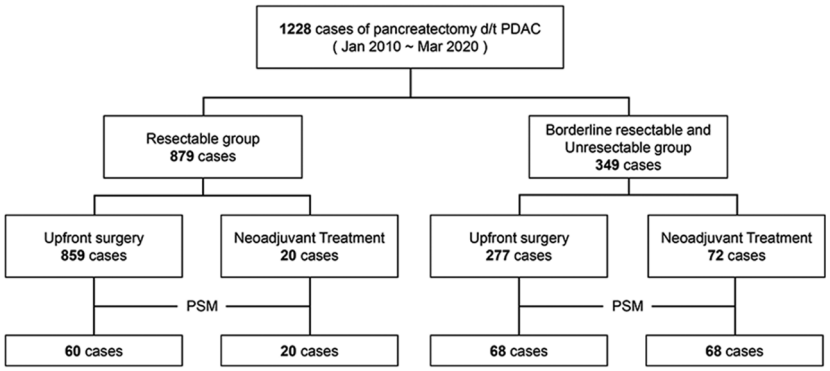


Figure 1. *The number of patients in study flow. PDAC: Pancreatic ductal adenocarcinoma; PSM: propensity score matching.*

NAT group (3.1 cm *versus* 2.8 cm). This tendency was not significant in RPC. The rate of vascular resection was significantly higher in the NAT group compared with the UpS group (55.0% *versus* 6.6%) in RPC, whereas vascular resection was significantly less performed in the NAT group than in the UpS group (34.7% *versus* 67.1%) in LAPC. All of the patients who underwent combined operation were in the UpS group, and none of them was in the NAT group. The rate of combined operation was 7.9% in the UpS group of LAPC, which was significant compared with the NAT group of LAPC. The combined operation was mostly attributed to resection of adjacent organs. Operation duration in the NAT group was significantly longer than that in the UpS group in RPC (322.8 min *versus* 273.1 min), whereas it was not significantly different in LAPC. More oncologic benefits of NAT were found in LAPC when compared with RPC. T stage and N stage were decreased. The rate of R0 resection was higher (76.4% *versus* 67.5%) and the rate of lymphovascular/perineural invasion was lower (30.6% *versus* 63.5%/66.6% *versus* 95.3%) in the NAT group than in the UpS group.

Age, whether patients had underlying DM or not, and initial tumor size that showed significant differences before PSM, were balanced after PSM conducted using these factors. The results of PSM of the six factors are shown in Table II.

Table III shows the PSM results of clinical characteristics excluding the six PSM factors, operative characteristics, pathological characteristics, and short-term postoperative outcomes in each group. The tendency of the rate of vascular resection and combined operation was still similar after PSM. The oncologic benefits of NAT observed in LAPC compared with RPC were similar after PSM. T stage, N stage, and the rate of lymphovascular/perineural invasion were significantly lower in the NAT group of LAPC. The rate of R0 resection was still higher, but was not significant.

*Short-term postoperative outcomes.* The short-term postoperative outcomes showed no significant differences between the UpS group and the NAT group in both RPC and LAPC. The outcomes before PSM are listed in Table I. The length of stay did not differ and was 12.5 days *versus* 11.6 days in RPC and 13.1 days *versus* 12.8 days in LAPC, respectively. Major complications and CR-POPF requiring special management in the immediate postoperative period were not at all frequent when NAT was administered first. The incidence of major complications was 19.2% *versus* 15.0% in RPC and 17.7% *versus* 16.7% in LAPC, and that of CR-POPF was 6.6% *versus* 5.3% in RPC and 3.5% *versus* 3.0% in LAPC. Both the readmission rates within 30-days and 90-days after surgery showed no significant differences between the UpS group and the NAT group, regardless of RPC or LAPC. Likewise, there were no differences in mortality both within 30-days and 90-days.

Table III shows that the results of all short-term postoperative outcomes were still similar even after PSM. When NAT was administered, regardless of the classification of patients into RPC or LAPC, no significant increase in complications was detected in the short-term postoperative period.

## Discussion

It is widely accepted that pancreatic cancer is a systemic disease and systemic therapy is important (14-16). As a pancreatic cancer treatment strategy, most of the systemic therapies had been performed after resection (17-20). Then, the effectiveness of NAT emerged, and has been increasingly performed (23-31). This study showed that NAT has been increasingly practiced in our center and included patients who underwent pancreatectomy from January 2010 to March 2020. The frequency of NAT increased abruptly in 2017 and has been steadily increasing since then, even though the frequency of upfront pancreatectomy has been almost the same since around 2013.

In LAPC, it was revealed that there was a significant oncologic benefit from NAT such as downstaging, despite the

Table I. *Clinical, operative, pathological characteristics and short-term postoperative outcomes [Mean±Standard deviation/number (percent)].*

| | RPC (n=879) | | | LAPC (n=349) | | |
|---|---|---|---|---|---|---|
| | UpS group (n=859) | NAT group (n=20) | *p*-Value | UpS group (n=277) | NAT group (n=72) | *p*-Value |
| Age | 64.8±10.0 | 63.7±8.2 | 0.618 | 63.4±9.8 | 60.1±10.0 | **0.012** |
| Gender | | | 0.361 | | | 0.577 |
| Male | 498 (58.0) | 14 (70.0) | | 167 (60.3) | 46 (63.9) | |
| Female | 361 (42.0) | 6 (30.0) | | 110 (39.7) | 26 (36.1) | |
| Body weight (kg) | 60.8±9.9 | 62.2±10.1 | 0.541 | 59.9±9.5 | 62.7±10.0 | **0.026** |
| BMI (kg/m$^2$) | 23.2±3.1 | 23.1±2.8 | 0.871 | 22.7±2.8 | 23.4±3.0 | 0.094 |
| DM | | | **0.020** | | | 0.248 |
| No | 530 (61.7) | 7 (35.0) | | 168 (60.6) | 49 (68.1) | |
| Yes | 329 (38.3) | 13 (65.0) | | 109 (39.4) | 23 (31.9) | |
| ASA score | | | 1.000 | | | 0.159 |
| 1 | 110 (12.8) | 2 (10.0) | | 41 (14.8) | 5 (7.0) | |
| 2 | 657 (76.5) | 16 (80.0) | | 207 (74.7) | 61 (84.7) | |
| 3 | 92 (10.7) | 2 (10.0) | | 29 (10.5) | 6 (8.3) | |
| Preoperative CEA | | | 0.315 | | | 0.922 |
| Normal (≤5 ng/ml) | 628 (73.1) | 15 (75.0) | | 206 (74.4) | 52 (72.2) | |
| Elevated (>5 ng/ml) | 103 (12.0) | 4 (20.0) | | 27 (9.7) | 8 (11.1) | |
| Unknown | 128 (14.9) | 1 (5.0) | | 44 (15.9) | 12 (16.7) | |
| Preoperative CA19-9 | | | 0.416 | | | 0.072 |
| Normal (≤37 U/ml) | 292 (34.0) | 4 (20.0) | | 69 (24.9) | 26 (36.1) | |
| Elevated (>37 U/ml) | 546 (63.6) | 16 (80.0) | | 200 (72.2) | 46 (63.9) | |
| Unknown | 21 (2.4) | 0 (0.0) | | 8 (2.9) | 0 (0.0) | |
| Initial tumor size (cm) | 2.7±1.2 | 3.2±0.7 | 0.057 | 2.8±0.9 | 3.1±0.9 | **0.010** |
| Operation type | | | 0.468 | | | 0.258 |
| PPPD | 266 (31.0) | 9 (45.0) | | 106 (38.3) | 23 (31.9) | |
| PRPD | 222 (25.8) | 5 (25.0) | | 109 (39.3) | 27 (37.5) | |
| DP | 328 (38.2) | 5 (25.0) | | 39 (14.1) | 17 (23.7) | |
| TP | 43 (5.0) | 1 (5.0) | | 23 (8.3) | 5 (6.9) | |
| Vascular resection | | | **<0.001** | | | **<0.001** |
| No | 802 (93.4) | 9 (45.0) | | 91 (32.9) | 47 (65.3) | |
| Yes | 57 (6.6) | 11 (55.0) | | 186 (67.1) | 25 (34.7) | |
| Combined operation | | | 0.096 | | | **0.011** |
| No | 747 (87.0) | 20 (100.0) | | 255 (92.1) | 72 (100.0) | |
| Yes | 112 (13.0) | 0 (0.0) | | 22 (7.9) | 0 (0.0) | |
| Operation duration (minutes) | 273.1±83.4 | 322.8±72.2 | **0.008** | 348.0±83.9 | 349.4±100.6 | 0.899 |
| EBL (ml) | 384.4±356.2 | 1027.5±2202.4 | 0.207 | 584.5±627.4 | 601.4±685.7 | 0.842 |
| Differentiation | | | 0.299 | | | 0.247 |
| Well | 52 (6.1) | 1 (5.0) | | 11 (4.0) | 3 (4.1) | |
| Moderately | 564 (65.7) | 17 (85.0) | | 186 (67.1) | 49 (68.1) | |
| Poorly | 189 (22.0) | 1 (5.0) | | 73 (26.4) | 15 (20.8) | |
| Undifferentiated | 21 (2.4) | 0 (0.0) | | 3 (1.1) | 1 (1.4) | |
| Unknown | 33 (3.8) | 1 (5.0) | | 4 (1.4) | 4 (5.6) | |
| Tumor size | 3.0±1.6 | 2.8±1.0 | 0.621 | 3.2±1.3 | 2.3±1.2 | **<0.001** |
| T stage | | | 0.334 | | | **<0.001** |
| Tis | 1 (0.1) | 0 (0.0) | | 0 (0.0) | 0 (0.0) | |
| T1a | 3 (0.4) | 0 (0.0) | | 1 (0.4) | 6 (8.3) | |
| T1b | 7 (0.8) | 1 (5.0) | | 0 (0.0) | 4 (5.6) | |
| T1c | 192 (22.4) | 3 (15.0) | | 31 (11.2) | 18 (25.0) | |
| T2 | 532 (61.9) | 13 (65.0) | | 199 (71.8) | 40 (55.5) | |
| T3 | 124 (14.4) | 3 (15.0) | | 46 (16.6) | 4 (5.6) | |
| N stage | | | 0.461 | | | **<0.001** |
| N0 | 355 (41.3) | 11 (55.0) | | 77 (27.8) | 50 (69.4) | |
| N1 | 339 (39.5) | 7 (35.0) | | 134 (48.4) | 18 (25.0) | |
| N2 | 165 (19.2) | 2 (10.0) | | 66 (23.8) | 4 (5.6) | |
| Harvested LN | 18.7±10.7 | 18.9±10.5 | 0.964 | 21.6±10.9 | 16.7±8.2 | **<0.001** |
| Metastatic LN | 2.0±3.0 | 1.4±3.2 | 0.397 | 2.7±3.7 | 0.7±1.8 | **<0.001** |

Table I. *Continued*

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| | RPC (n=879) | | | LAPC (n=349) | | |
|---|---|---|---|---|---|---|
| | UpS group (n=859) | NAT group (n=20) | *p*-Value | UpS group (n=277) | NAT group (n=72) | *p*-Value |
| M stage | | | 1.000 | | | 1.000 |
| M0 | 848 (98.7) | 20 (100.0) | | 275 (99.3) | 72 (100.0) | |
| M1 | 11 (1.3) | 0 (0.0) | | 2 (0.7) | 0 (0.0) | |
| Resection margin | | | 0.820 | | | **0.003** |
| R0 | 691 (80.4) | 16 (80.0) | | 187 (67.5) | 55 (76.4) | |
| R1 | 159 (18.5) | 4 (20.0) | | 86 (31.1) | 12 (16.7) | |
| R2 | 9 (1.1) | 0 (0.0) | | 4 (1.4) | 5 (6.9) | |
| Lymphovascular invasion | | | 0.733 | | | **<0.001** |
| No | 308 (35.9) | 9 (45.0) | | 76 (27.4) | 44 (61.1) | |
| Yes | 438 (50.9) | 9 (45.0) | | 176 (63.5) | 22 (30.6) | |
| Unknown | 113 (13.2) | 2 (10.0) | | 25 (9.1) | 6 (8.3) | |
| Perineural invasion | | | 1.000 | | | **<0.001** |
| No | 88 (10.2) | 2 (10.0) | | 10 (3.6) | 21 (29.2) | |
| Yes | 737 (85.8) | 18 (90.0) | | 264 (95.3) | 48 (66.6) | |
| Unknown | 34 (4.0) | 0 (0.0) | | 3 (1.1) | 3 (4.2) | |
| Length of stay (days) | 12.5±9.3 | 11.6±4.9 | 0.666 | 13.1±7.9 | 12.8±8.3 | 0.827 |
| Clavien-Dindo classification | | | 0.794 | | | 0.132 |
| No complication | 472 (54.9) | 11 (55.0) | | 139 (50.2) | 40 (55.6) | |
| Minor | | | | | | |
| I | 53 (6.2) | 2 (10.0) | | 25 (9.0) | 6 (8.3) | |
| II | 169 (19.7) | 4 (20.0) | | 64 (23.1) | 14 (19.4) | |
| Major | | | | | | |
| IIIa | 119 (13.9) | 2 (10.0) | | 37 (13.3) | 7 (9.7) | |
| IIIb | 19 (2.2) | 1 (5.0) | | 1 (0.4) | 4 (5.6) | |
| IVa | 18 (2.1) | 0 (0.0) | | 6 (2.2) | 1 (1.4) | |
| IVb | 2 (0.2) | 0 (0.0) | | 1 (0.4) | 0 (0.0) | |
| V | 7 (0.8) | 0 (0.0) | | 4 (1.4) | 0 (0.0) | |
| POPF | n=816 | n=19 | 1.000 | n=254 | n=67 | 1.000 |
| No (biochemical leak) | 762 (93.4) | 18 (94.7) | | 245 (96.5) | 65 (97.0) | |
| CR-POPF | | | | | | |
| Grade B | 49 (6.0) | 1 (5.3) | | 7 (2.7) | 2 (3.0) | |
| Grade C | 5 (0.6) | 0 (0.0) | | 2 (0.8) | 0 (0.0) | |
| TP | 43 | 1 | | 23 | 5 | |
| 30-day unplanned readmission | 62 (7.2) | 1 (5.0) | 1.000 | 13 (4.7) | 5 (6.9) | 0.548 |
| 90-day unplanned readmission | 100 (11.6) | 1 (5.0) | 0.719 | 24 (8.7) | 8 (11.1) | 0.498 |
| 30-day mortality | 4 (0.5) | 0 (0.0) | 1.000 | 2 (0.7) | 0 (0.0) | 1.000 |
| 90-day mortality | 11 (1.3) | 1 (5.0) | 0.243 | 7 (2.5) | 1 (1.4) | 1.000 |

BMI: Body mass index; DM: diabetes mellitus; ASA: American society of anesthesiologists; CEA: carcinoembryonic antigen; CA19-9: Carbohydrate antigen 19-9; PPPD: pylorus preserving pancreaticoduodenectomy; PRPD: pylorus resecting pancreaticoduodenectomy; DP: distal pancreatectomy; TP: total pancreatectomy; EBL: estimated blood loss; LN: lymph node; POPF: postoperative pancreatic fistula; CR-POPF: clinically relevant POPF; UpS: upfront surgery; NAT: neoadjuvant treatment; RPC: resectable pancreatic cancer; LAPC: locally advanced pancreatic cancer. Bold *p*-Values are considered statistically significant ($p<0.05$).

fact that the patients who underwent NAT had a significantly larger tumor at the time of diagnosis. NAT appeared to be effective oncologically in RPC as well, but its significance was poor. The results of short-term postoperative outcomes including general major complications and CR-POPF showed no significant differences between the UpS and the NAT groups in both RPC and LAPC.

The NAT group included 20 cases in RPC, which was quite a lot when compared to 72 cases in LAPC. We believe that because NAT was administered due to PV or SMV invasion, and cases which contact angle of invaded vessel was less than 180˚, were classified as RPC according to the NCCN guidelines (20). Since many studies have demonstrated the preferable outcomes of NAT in RPC, it is expected that NAT will be administered to more RPC patients in the future (28-31).

In LAPC, the high rate of combined operation in the UpS group was significant when compared with the NAT group. Most of these cases were subjected to resection of adjacent

Table II. *Matching factors after PSM [Mean±Standard deviation/number (percent)].*

| | RPC (n=80) | | | LAPC (n=136) | | |
|---|---|---|---|---|---|---|
| | UpS group (n=60) | NAT group (n=20) | *p*-Value | UpS group (n=68) | NAT group (n=68) | *p*-Value |
| Age | 64.3±10.0 | 63.7±8.2 | 0.799 | 60.6±9.5 | 61.1±9.4 | 0.759 |
| Gender | | | 1.000 | | | 1.000 |
| Male | 42 (70.0) | 14 (70.0) | | 43 (63.2) | 42 (61.8) | |
| Female | 18 (30.0) | 6 (30.0) | | 25 (36.8) | 26 (38.2) | |
| BMI (kg/m$^2$) | 22.8±2.8 | 23.1±2.8 | 0.697 | 23.1±3.3 | 23.2±3.0 | 0.863 |
| DM | | | 1.000 | | | 0.721 |
| No | 21 (35.0) | 7 (35.0) | | 42 (61.8) | 45 (66.2) | |
| Yes | 39 (65.0) | 13 (65.0) | | 26 (38.2) | 23 (33.8) | |
| ASA score | | | 0.880 | | | 1.000 |
| 1 | 6 (10.0) | 2 (10.0) | | 4 (5.9) | 5 (7.4) | |
| 2 | 50 (83.3) | 16 (80.0) | | 57 (83.8) | 57 (83.8) | |
| 3 | 4 (6.7) | 2 (10.0) | | 7 (10.3) | 6 (8.8) | |
| Initial tumor size (cm) | 3.1±1.1 | 3.2±0.7 | 0.754 | 3.1±1.1 | 3.1±0.9 | 0.709 |

PSM: Propensity score matching; NAT: neoadjuvant treatment; UpS: upfront surgery; RPC: resectable pancreatic cancer; LAPC: locally advanced pancreatic cancer; BMI: body mass index; DM: diabetes mellitus; ASA: American society of anesthesiologists.

organs involved by a locally advanced tumor. There were also a few cases that combined operation was performed in order to manage an accidently occurring injury, possibly due to a locally advanced tumor.

There was a significant difference in the tendency of vascular resection between RPC and LAPC. The rate of vascular resection was very low in the UpS group in RPC, as expected. It was found that there were more patients whose invaded vessel should be eventually resected during conversion surgery in the NAT group belonging to RPC. On the other hand, in LAPC, when upfront surgery was performed, the rate of resection of the invaded vessel was higher. Also, when NAT was first administered in LAPC, the rate of vascular resection was low; this is an oncologic benefit of NAT (24, 25).

However, this point may be a limitation involving selection bias in our study. There are certainly many NAT cases that did not undergo conversion surgery or were lost. It was very likely that they were more advanced or susceptible to complications due to a generally poor clinical condition. If they had conversion surgery, the rate of vascular resection would have risen considerably, and the short-term postoperative outcomes might also be found to be significantly different when compared with the UpS group.

Because this was a retrospective study and the data were entirely based on medical records of our center, this study has some limitations. There might exist some information that we were not able to collect from the medical records. That is because there must have been patients whose follow-up was not continuous and lost.

Although there might be these limitations, except for three patients whose drain amylase levels were unmeasured, almost all of included patients were investigated to determine the occurrence of POPF, a major short-term postoperative complication after pancreatectomy. Because it has been a routine practice to measure drainage amylase levels on the third day after surgery in all patients who underwent any pancreatectomy. Also, it could be stated that data of 30-days mortality and 90-days mortality were accurate since the Department of Medical Records in our center collects information on the fact and date of death from the government departments and includes it in the electronic medical records.

Through this retrospectively descriptive study, we were able to identify the patients who received NAT for PDAC in our high-volume single center. Data on the short-term postoperative outcomes, the purpose of this study, were searched and analyzed. It was confirmed that there were no significant differences between the cases of upfront surgery and the cases of NAT followed by surgery.

## Conclusion

In cases where NAT was performed followed by the surgery, the short-term postoperative (90 days) outcomes were comparable to those of upfront surgery cases. We concluded that it is reasonable to perform conversion surgery for PDAC patients who underwent NAT. This can be applied regardless of whether patients are included in resectable, borderline resectable, or unresectable status at the time of PDAC diagnosis.

In the future, we plan to investigate the long-term postoperative outcomes in our center. If it can be confirmed that the long-term outcomes are also favorable in the cases of

Table III. *Clinical, operative, pathological characteristics and short-term postoperative outcomes after PSM [Mean±Standard deviation/number (percent)].*

| | RPC (n=80) | | | LAPC (n=136) | | |
|---|---|---|---|---|---|---|
| | UpS group (n=60) | NAT group (n=20) | *p*-Value | UpS group (n=68) | NAT group (n=68) | *p*-Value |
| Body weight (kg) | 61.5±10.6 | 62.2±10.1 | 0.816 | 61.7±10.6 | 61.9±9.4 | 0.951 |
| Preoperative CEA | | | 0.465 | | | 0.730 |
| Normal (≤5 ng/ml) | 42 (70.0) | 15 (75.0) | | 48 (70.6) | 49 (72.0) | |
| Elevated (>5 ng/ml) | 8 (13.3) | 4 (20.0) | | 6 (8.8) | 8 (11.8) | |
| Unknown | 10 (16.7) | 1 (5.0) | | 14 (20.6) | 11 (16.2) | |
| Preoperative CA19-9 | | | 0.363 | | | 0.052 |
| Normal (≤37 U/ml) | 20 (33.3) | 4 (20.0) | | 16 (23.5) | 25 (36.8) | |
| Elevated (>37 U/ml) | 38 (63.4) | 16 (80.0) | | 49 (72.1) | 43 (63.2) | |
| Unknown | 2 (3.3) | 0 (0.0) | | 3 (4.4) | 0 (0.0) | |
| Operation type | | | 0.240 | | | 0.363 |
| PPPD | 13 (21.7) | 9 (45.0) | | 29 (42.6) | 20 (29.4) | |
| PRPD | 24 (40.0) | 5 (25.0) | | 23 (33.8) | 26 (38.2) | |
| DP | 20 (33.3) | 5 (25.0) | | 11 (16.2) | 17 (25.0) | |
| TP | 3 (5.0) | 1 (5.0) | | 5 (7.4) | 5 (7.4) | |
| Vascular resection | | | **<0.001** | | | **<0.001** |
| No | 55 (91.7) | 9 (45.0) | | 20 (29.4) | 45 (66.2) | |
| Yes | 5 (8.3) | 11 (55.0) | | 48 (70.6) | 23 (33.8) | |
| Combined operation | | | 0.059 | | | **<0.001** |
| No | 50 (83.3) | 20 (100.0) | | 57 (83.8) | 68 (100.0) | |
| Yes | 10 (16.7) | 0 (0.0) | | 11 (16.2) | 0 (0.0) | |
| Operation duration (minutes) | 287.7±79.2 | 322.8±72.2 | 0.083 | 351.1±89.7 | 350.1±102.7 | 0.953 |
| EBL (ml) | 505.8±703.3 | 1027.5±2202.4 | 0.109 | 521.3±317.6 | 614.7±703.0 | 0.321 |
| Differentiation | | | **0.024** | | | 0.640 |
| Well | 1 (1.7) | 1 (5.0) | | 4 (5.9) | 3 (4.4) | |
| Moderately | 42 (70.0) | 17 (85.0) | | 52 (76.5) | 46 (67.6) | |
| Poorly | 17 (28.3) | 1 (5.0) | | 10 (14.7) | 14 (20.6) | |
| Undifferentiated | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 1 (1.5) | |
| Unknown | 0 (0.0) | 1 (5.0) | | 2 (2.9) | 4 (5.9) | |
| Tumor size | 3.2±1.2 | 2.8±1.0 | 0.290 | 3.6±2.0 | 2.3±1.2 | **<0.001** |
| T stage | | | 0.490 | | | **<0.001** |
| Tis | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 0 (0.0) | |
| T1a | 0 (0.0) | 0 (0.0) | | 1 (1.5) | 6 (8.8) | |
| T1b | 0 (0.0) | 1 (5.0) | | 0 (0.0) | 4 (5.9) | |
| T1c | 10 (16.7) | 3 (15.0) | | 6 (8.8) | 15 (22.0) | |
| T2 | 39 (65.0) | 13 (65.0) | | 44 (64.7) | 39 (57.4) | |
| T3 | 11 (18.3) | 3 (15.0) | | 17 (25.0) | 4 (5.9) | |
| N stage | | | 0.375 | | | **<0.001** |
| N0 | 24 (40.0) | 11 (55.0) | | 19 (28.0) | 46 (67.6) | |
| N1 | 22 (36.7) | 7 (35.0) | | 33 (48.5) | 18 (26.5) | |
| N2 | 14 (23.3) | 2 (10.0) | | 16 (23.5) | 4 (5.9) | |
| Harvested LN | 18.2±11.1 | 18.9±10.5 | 0.828 | 22.8±12.5 | 16.7±8.3 | **0.001** |
| Metastatic LN | 1.9±2.6 | 1.4±3.2 | 0.472 | 2.9±5.3 | 0.8±1.8 | **0.002** |
| M stage | | | 1.000 | | | 1.000 |
| M0 | 59 (98.3) | 20 (100.0) | | 67 (98.5) | 68 (100.0) | |
| M1 | 1 (1.7) | 0 (0.0) | | 1 (1.5) | 0 (0.0) | |
| Resection margin | | | 0.566 | | | 0.197 |
| R0 | 43 (71.7) | 16 (80.0) | | 46 (67.7) | 52 (76.5) | |
| R1 | 17 (28.3) | 4 (20.0) | | 20 (29.4) | 12 (17.6) | |
| R2 | 0 (0.0) | 0 (0.0) | | 2 (2.9) | 4 (5.9) | |
| Lymphovascular invasion | | | 0.578 | | | **0.001** |
| No | 20 (33.3) | 9 (45.0) | | 20 (29.4) | 40 (58.8) | |
| Yes | 35 (58.4) | 9 (45.0) | | 42 (61.8) | 22 (32.4) | |
| Unknown | 5 (8.3) | 2 (10.0) | | 6 (8.8) | 6 (8.8) | |
| Perineural invasion | | | 0.697 | | | **<0.001** |
| No | 3 (5.0) | 2 (10.0) | | 2 (2.9) | 19 (27.9) | |
| Yes | 56 (93.3) | 18 (90.0) | | 64 (94.2) | 46 (67.7) | |
| Unknown | 1 (1.7) | 0 (0.0) | | 2 (2.9) | 3 (4.4) | |

Table III. *Continued*

Table III. *Continued*

| | RPC (n=80) | | | LAPC (n=136) | | |
|---|---|---|---|---|---|---|
| | UpS group (n=60) | NAT group (n=20) | *p*-Value | UpS group (n=68) | NAT group (n=68) | *p*-Value |
| Length of stay (days) | 14.0±11.6 | 11.6±4.9 | 0.374 | 12.6±5.9 | 12.9±8.4 | 0.842 |
| Clavien-Dindo classification | | | 0.648 | | | 0.065 |
| No complication | 33 (55.0) | 11 (55.0) | | 30 (44.1) | 37 (54.4) | |
| Minor | | | | | | |
| I | 2 (3.3) | 2 (10.0) | | 4 (5.9) | 6 (8.8) | |
| II | 12 (20.0) | 4 (20.0) | | 18 (26.5) | 13 (19.1) | |
| Major | | | | | | |
| IIIa | 10 (16.7) | 2 (10.0) | | 15 (22.0) | 7 (10.3) | |
| IIIb | 1 (1.7) | 1 (5.0) | | 0 (0.0) | 4 (5.9) | |
| IVa | 2 (3.3) | 0 (0.0) | | 0 (0.0) | 1 (1.5) | |
| IVb | 0 (0.0) | 0 (0.0) | | 1 (1.5) | 0 (0.0) | |
| V | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 0 (0.0) | |
| POPF | n=57 | n=19 | 1.000 | n=63 | n=63 | 1.000 |
| No (biochemical leak) | 53 (93.0) | 18 (94.7) | | 61 (96.8) | 61 (96.8) | |
| CR-POPF | | | | | | |
| Grade B | 3 (5.3) | 1 (5.3) | | 1 (1.6) | 2 (3.2) | |
| Grade C | 1 (1.7) | 0 (0.0) | | 1 (1.6) | 0 (0.0) | |
| TP | 3 | 1 | | 5 | 5 | |
| 30-day unplanned readmission | 6 (10.0) | 1 (5.0) | 0.673 | 6 (8.8) | 4 (5.9) | 0.744 |
| 90-day unplanned readmission | 10 (16.7) | 1 (5.0) | 0.275 | 8 (11.8) | 7 (10.3) | 1.000 |
| 30-day mortality | 0 (0.0) | 0 (0.0) | - | 0 (0.0) | 0 (0.0) | - |
| 90-day mortality | 0 (0.0) | 1 (5.0) | 0.250 | 0 (0.0) | 1 (1.5) | 1.000 |

PSM: Propensity score matching; NAT: neoadjuvant treatment; UpS: upfront surgery; RPC: resectable pancreatic cancer; LAPC: locally advanced pancreatic cancer; CEA: carcinoembryonic antigen; CA19-9: Carbohydrate antigen 19-9; PPPD: pylorus preserving pancreaticoduodenectomy; PRPD: pylorus resecting pancreaticoduodenectomy; DP: distal pancreatectomy; TP: total pancreatectomy; EBL: estimated blood loss; LN: lymph node; POPF: postoperative pancreatic fistula; CR-POPF: clinically relevant POPF. Bold *p*-Values are considered statistically significant ($p<0.05$).

NAT followed by surgery in our high-volume single center, it will contribute to standardize PDAC treatment strategies.

## Conflicts of Interest

The Authors declare no conflicts of interest, financial or otherwise, in relation to this study.

## Authors' Contributions

Conception/design: Jin Seok Heo, Sang Hyun Shin, and Ji Hye Jung; Provision of study material or patients: Ji Hye Jung, So Kyung Yoon, and Sang Hyun Shin; Collection and assembly of data: Ji Hye Jung, So Jeong Yoon, and In Woong Han; Data analysis and interpretation: Ji Hye Jung, So Kyung Yoon, and Jin Seok Heo; Manuscript writing: Ji Hye Jung, Sang Hyun Shin, and Jin Seok Heo. All Authors have read and approved the final manuscript.

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