**Table I**

Clinicopathological characteristics of the whole cohort

|  |  |
| --- | --- |
| Characteristic | Patients(n=612)[%] |
| Sex |  |
| Male | 352[57.5] |
| Female | 260[42.5] |
| Age median(range)(year) | 61(31-82) |
| CA19-9 median(range) (U/ml) | 156.25(0.6-178850.00) |
| CEA median(range) (ng/ml) | 3.3550(0.20-3032.00) |
| CA242 median(range) (U/ml) | 19.64(0.19-11237.00) |
| Tumor location |  |
| Head | 416[68] |
| Body and tail | 196[32] |
| Surgery |  |
| Pancreaticoduodenectomy | 414[67.6] |
| Distal pancreatectomy | 195[31.9] |
| Total pancreatectomy | 3[0.5] |
| TNM stage |  |
| I | 233[38.1] |
| II | 285[46.6] |
| III | 94[15.4] |
| T stage |  |
| T1 | 99[16.2] |
| T2 | 323[52.8] |
| T3 | 175[28.6] |
| T4 | 15[2.5] |
| N stage |  |
| N0 | 343[56.0] |
| N1 | 191[31.2] |
| N2 | 78[12.7] |
| Histology grade |  |
| Low grade | 264[43.1] |
| Well differentiation | 23[3.8] |
| Moderate differentiation | 241[39.4] |
| High grade | 348[56.9] |
| Poor differentiation | 348[56.9] |
| Undifferentiation | 0 |
| Perineural invasion |  |
| No | 249[40.7] |
| Yes | 363[59.3] |
| Lymphovascular invasion |  |
| No | 458[74.8] |
| Yes | 154[25.2] |
| Chemotherapy regime |  |
| None | 311[50.8] |
| GS | 80[26.6] |
| GEMOX | 68[22.6] |
| GEM | 61[20.3] |
| AG | 33[11] |
| S-1 | 47[15.6] |
| FOLFIRINOX | 12[4.0] |
| Overall survival median(range)(months) | 18(6-126) |

CA19-9:carbohydrate antigen 19-9;CEA:carcinoembryonic antigen;CA242:carbohydrate antigen 242; TNM stage:the tumor, node and metastasis staging system; GS: gemcitabine and S-1; GEMOX: gemcitabine and oxaliplatin; GEM: gemcitabine; AG: albumin-bound paclitaxel and gemcitabine; FOLFIRINOX:a combination therapy consisting of 5-FU/leucovorin plus oxaliplatin and irinotecan.

**Table II**

Univariate and multivariate survival analysis of all the patients with PDAC

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristics | n | 5-year  OS(%) | Univariate analysis | |  | Multivariate analysis | |
| HR(95% CI) | P |  | HR(95% CI) | P |
| Sex |  | | | | | | |
| Male | 352 | 18.5 | 1(ref) |  |  |  |  |
| Female | 260 | 18.6 | 1.118(0.92-1.358) | 0.264 |  |  |  |
| Age at surgery(year) |  |  |  |  |  |  |  |
| <70 | 525 | 19.9 | 1(ref) |  |  | 1(ref) |  |
| ≥70 | 87 | 9.2 | 1.430(1.010-1.857) | 0.007 |  | 1.546(1.184-2.020) | 0.001 |
| CA199 (U/ml) |  |  |  |  |  |  |  |
| ≤112 | 252 | 22.6 | 1(ref) |  |  | 1(ref) |  |
| >112 | 360 | 15.9 | 1.458(1.196-1.778) | <0.001 |  | 1.355(1.098-1.671) | 0.005 |
| CEA (ng/ml) |  |  |  |  |  |  |  |
| ≤5 | 432 | 21.7 | 1(ref) |  |  | 1(ref) |  |
| >5 | 180 | 12.2 | 1.412(1.146-1.740) | 0.001 |  | 1.199(0.956-1.504) | 0.116 |
| Postoperative chemotherapy |  |  |  |  |  |  |  |
| Yes | 301 | 24.2 | 1(ref) |  |  | 1(ref) |  |
| No | 311 | 14.1 | 1.664(1.372-2.018) | <0.001 |  | 1.696(1.396-2.061) | <0.001 |
| TNM stage |  |  |  |  |  |  |  |
| I | 233 | 28.2 | 1(ref) |  |  | 1(ref) |  |
| II | 285 | 14.9 | 1.531(1.235-1.897) | <0.001 |  | 1.440(1.153-1.798) | 0.001 |
| III | 94 | 7.7 | 2.279(1.720-3.019) | <0.001 |  | 2.140(1.565-2.925) | <0.001 |
| Histology grade |  |  |  |  |  |  |  |
| Low grade | 264 | 23.5 | 1(ref) |  |  | 1(ref) |  |
| High grade | 348 | 15.7 | 1.642(1.348-1.999) | <0.001 |  | 1.545(1.265-1.887) | <0.001 |
| Tumor location |  |  |  |  |  |  |  |
| Head | 416 | 19.6 | 1(ref) |  |  |  |  |
| Body and tail | 196 | 18.2 | 0.998(0.811-1.227) | 0.983 |  |  |  |
| Perineural invasion |  |  |  |  |  |  |  |
| No | 249 | 25.3 | 1(ref) |  |  | 1(ref) |  |
| Yes | 363 | 13.3 | 1.222(1.004-1.487) | 0.046 |  | 1.014(0.827-1.243) | 0.895 |
| Lymphovascular invasion |  |  |  |  |  |  |  |
| No | 458 | 20.9 | 1(ref) |  |  | 1(ref) |  |
| Yes | 154 | 14 | 1.432(1.155-1.774) | 0.001 |  | 1.101(0.867-1.397) | 0.430 |

Low grade: well and moderate differentiation; high grade: poor differentiation and undifferentiation; OS: overall survival; HR: hazard ratio; 95% CI:95% confidence interval.

**Table III**

Multivariate survival analyses of all PDAC patients after including biological risk and mTNM,respectively

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Factors | | Multivariate analysis  (include biological risk) | | |  | Multivariate analysis  (both include mTNM and biological risk) | | |
| HR | 95%CI | P |  | HR | 95%CI | P |
| Age(year) | <70/≥70 | 1.522 | 1.165-1.988 | 0.002 |  | 1.516 | 1.162-1.977 | 0.002 |
| CA19-9(U/ml) | ≤112/>112 | 0.899 | 0.572-1.416 | 0.647 |  | - | - | - |
| CEA(ng/ml)) | ≤5/>5 | 1.221 | 0.974-1.531 | 0.084 |  | 1.173 | 0.940-1.463 | 0.158 |
| Histology grade | Low/High | 1.021 | 0.651-1.603 | 0.926 |  | - | - | - |
| TNM stage | I/II/III | 1.458 | 1.253-1.697 | <0.001 |  | 1.140 | 0.874-1.487 | 0.333 |
| Perineural invasion | No/Yes | 0.998 | 0.814-1.223 | 0.985 |  | 0.986 | 0.804-1.209 | 0.891 |
| Lymphvascular invasion | No/Yes | 1.073 | 0.848-1.359 | 0.557 |  | 1.072 | 0.847-1.357 | 0.563 |
| Postoperative chemotherapy | Yes/No | 1.687 | 1.389-2.049 | <0.001 |  | 1.668 | 1.373-2.026 | <0.001 |
| Biological risk | Low/Middle/High | 1.342 | 1.004-1.795 | 0.047 |  | 1.136 | 0.970-1.330 | 0.112 |
| mTNM stage | mI/mII/mIII | - | - | - |  | 1.389 | 1.041-1.853 | 0.025 |

Histology grade:Low, well and moderate differentiation; high, poor differentiation and undifferentiation. Biological risk: Low, CA199≤112 U/ml + low grade; Middle, CA19-9≤112 U/ml + high grade or CA19-9>112 U/ml + low grade; High, CA19-9>112 U/ml + high grade.

**Table IV**

PDAC patients were divided into three groups according to the biological risk of PDAC: Low, CA199≤112 U/ml + low grade; Middle, CA19-9≤112 U/ml + high grade or CA19-9>112 U/ml + low grade; High, CA19-9>112 U/ml + high grade

|  |  |  |  |
| --- | --- | --- | --- |
| Biological risk | I | II | III |
| Low | mI | mI | mIII |
| Middle | mI | mII | mIII |
| High | mII | mIII | mIII |

The biological risk was incorporated into the eighth edition of TNM staging system and composed the newly modified TNM (mTNM) stage.

**Table V**

The impact of mTNM and TNM on the prognostic value of staging

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristics | n | 5-year  OS(%) | Univariate analysis | |  | Multivariate analysis | | -2log likelihood |
| χ2 | P |  | HR(95% CI) | P |
| mTNM stage |  |  | 78.603 | <0.001 |  |  |  | 4688.361 |
| mI | 213 | 31.2 |  |  |  | 1(ref) | <0.001 |  |
| mII | 197 | 17.2 |  |  |  | 1.627(1.198-2.210) | 0.002 |  |
| mIII | 202 | 7.2 |  |  |  | 2.602(1.840-3.678) | <0.001 |  |
| TNM stage |  |  | 37.794 | <0.001 |  |  |  | 4694.876 |
| I | 233 | 28.2 |  |  |  | 1(ref) | <0.001 |  |
| II | 285 | 14.9 |  |  |  | 1.442(1.155-1.800) | 0.001 |  |
| III | 94 | 7.7 |  |  |  | 2.137(1.564-2.921) | <0.001 |  |

OS: overall survival; HR: hazard ratio; 95% CI:95% confidence interval.