

# Survival Analysis after Cephalic Pancreatoduodenectomy for Carcinoma of the Ampulla of Vater

Tudor A<sup>1</sup>, Molnar C<sup>1</sup>, Man A<sup>2</sup>, Tudor Bianca<sup>2</sup>, Roșca C<sup>3</sup>, Copotoiu C<sup>4</sup>

<sup>1</sup> Department of Anatomy and Embriology, University of Medicine and Pharmacy, Tîrgu Mureș, Romania

<sup>2</sup> Department of Microbiology, University of Medicine and Pharmacy, Tîrgu Mureș, Romania

<sup>3</sup> Surgery Clinic 1, Emergency County Hospital, Tîrgu Mureș, Romania

<sup>4</sup> Department of Surgery, University of Medicine and Pharmacy, Tîrgu Mureș, Romania

**Background:** Ampulla Vater carcinoma is a rare condition, having the best prognosis in periampullary malignant tumors. The purpose of this paper is to analyze the factors involved in long term survival after duodenopancreatectomy for carcinoma of the ampulla of Vater.

**Material and method:** This paper is a retrospective study across a 15-year period (1995–2009), during which 130 interventions for ampullary vaterian carcinoma were performed in Surgery Clinic I Tîrgu Mureș and Surgery Clinic III Cluj-Napoca. Cephalic pancreatoduodenectomy was performed in 86 cases, and we have obtained informations regarding late postoperative survival in 63 cases. The data was processed in Microsoft Excel, and the statistical analysis was performed with SPSS v. 17 for Windows. The threshold of significance was  $p < 0.05$ .

**Results:** Survival at 5 years after cephalic pancreatoduodenectomy, in the group analyzed (63 cases) was 43.1%.

We found a higher percentage of survival rate at 5 years for stage T1 tumors (tumor limited to the ampulla of Vater or sphincter of Oddi) - 68.3%, in the absence of regional adenopathies N0 - 68.3%, well differentiated tumors G1 - 90.5%, in tubulo-papillary adenocarcinoma histological type - 66.6%, in patients without lymphovascular invasion - 91.3% and in those without perineural invasion - 82.3%.

Multivariate analysis of prognostic factors shows a high risk of death in the presence of lymphovascular invasion ( $p = 0.0031$ ).

**Conclusions:** 1. Survival at 5 years after cephalic pancreatoduodenectomy was 43.1%, which is influenced by tumor extension, the presence of regional lymphadenopathy, the histopathological type of tumor, the degree of tumor differentiation, the lymphovascular or perineural invasion. 2. Multivariate analysis of prognostic factors shows that lymphovascular invasion is statistically significant in postoperative survival.

**Keywords:** ampulla of Vater, carcinoma, survival factors, pancreatoduodenectomy

## Introduction

Carcinoma of the ampulla of Vater includes a heterogeneous group of neoplasia originating in the ampulla of Vater or structures less than 1 cm around it, including: ampullary cancer, juxtapapillary D2 duodenum cancer, terminal bile duct cancer and juxtapapillary cephalopancreatic cancer. Ampullary carcinoma incidence is lower compared with cancer of the head of pancreas. Standard surgical procedure is the cephalic pancreatoduodenectomy.

The aim of this paper is to evaluate the factors involved in long term survival after cephalic pancreatoduodenectomy (DPC) performed for carcinoma of the ampulla of Vater.

## Material and method

This paper is a retrospective study across a 15 years period (1995–2009), based on the primary data obtained from records of patients admitted and operated with the diagnosis of carcinoma of ampulla of Vater in Surgery Clinic I from Tîrgu Mureș and Surgery Clinic III from Cluj-Napoca. In this period, 130 patients were operated with Vaterian ampullary carcinoma. There were performed 86 cephalic pancreatoduodenectomies, 4 ampullectomies, 19 bilio-digestive diversions and 21 exploratory laparotomies. Of the entire studied group (130 patients), we obtained information from 88 patients, also with the help of the oncology department and service records of population. Of the total interventions with radical intention (86 cases),

informations were obtained in 63 patients, and for the rest of the interventions (ampullectomies, bilio-digestive diversions, exploratory laparotomies) data were obtained for 25 of 44 cases. The data were processed in Microsoft Excel, and the statistical analysis was performed with SPSS v. 17 for Windows (Statistical Package for the Social Sciences, Chicago, Illinois). The existence of statistically significant differences between the various subgroups was tested using parametric or non-parametric tests. Kaplan Meier survival curves and multivariate regressions were used. The threshold of significance was  $p < 0.05$ . For continuous variables, medium values were expressed as medium  $\pm$  standard error of medium (SEM) or standard deviation (SD).

Patients admitted in emergency or in elective conditions for obstructive jaundice were included, and for whom, by further laboratory investigations, malignant etiology has been established. Only those patients were included in the study who have been examined by ultrasound, computer tomography, magnetic resonance or endoscopic retrograde cholangiopancreatography. Also, another inclusion criterion was the surgically confirmation by macroscopic aspect and/or by histological examination.

Patients who, have not been able to make preoperatively complex investigations were not included in the study. Several parameters that may influence survival were analyzed: T (primary tumor), N (regional lymph node invasion), tumor histological type, G (degree of tumor differentiation), lymphovascular invasion and perineu-

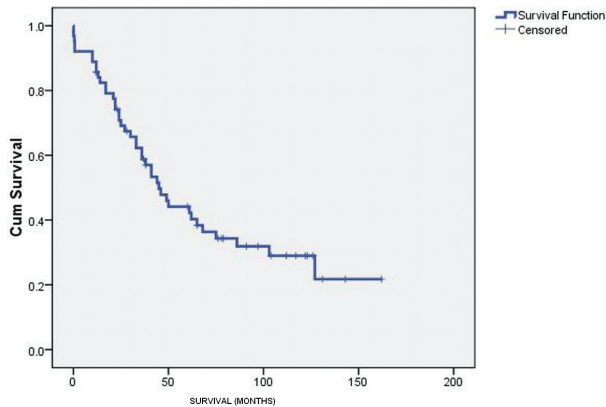


Fig. 1. Survival curve for the entire group of patients

ral invasion. Patient's data were used with their consent and were treated confidentially. The patients were asked for their consent to perform surgery, endoscopic or interventional radiological procedures, and the complications, risks and effects on quality of life have been explained in detail.

## Results

Survival at 5 years after DPC for the analyzed group (63 cases) was 43.1%, with an average survival of 69.89 months (54.2 to 85.5 months at 95% confidence interval – CI) (Figure 1).

Survival at 5 years after DPC depending on the T parameter showed a 68.3% survival for T1 cases (19 cases, 30.2%), 33.2% for T2 cases (21 patients, 33.3%), 20.4% for T3 cases (17 cases, 27%) and 15.8% for T4 cases (6 patients, 9.5%) (Figure 2).

Statistical study of regional lymph nodes invasion showed a 5-year survival after DPC of 68.3% in the cases without regional lymph node invasion (33 cases, 52.4%) and 13.9% (30 patients, 47.6%) respectively, in the cases with regional lymph node invasion (Figure 3).

G1 well differentiated tumors (20 cases, 31.7%) had a survival at five years after DPC of 90.5%, medium dif-

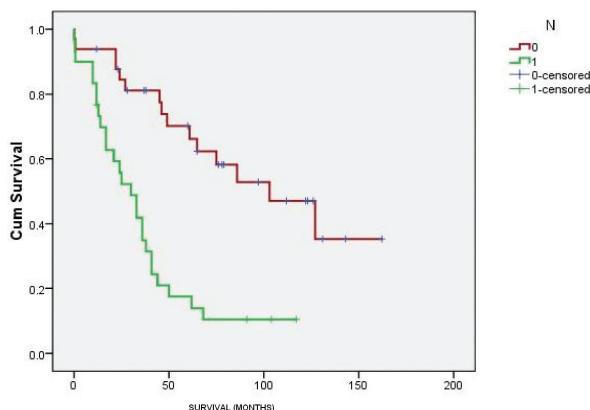


Fig. 3. Survival at 5 years after cephalic pancreatoduodenectomy depending on the N parameter

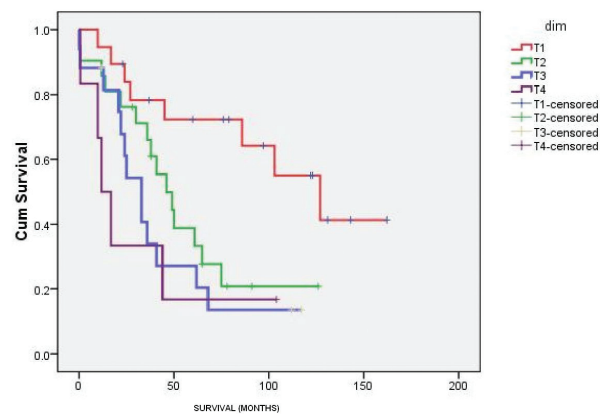


Fig. 2. Survival at 5 years after cephalic pancreatoduodenectomy depending on the T parameter

ferentiated G2 tumors (33 cases, 52.4%) had a survival of 18.2%, poorly differentiated G3 tumors (8 cases, 12.7%) and patients with undifferentiated G4 (2 cases, 3.2%) did not survive 5 years (Figure 4).

Cases with mucinous adenocarcinoma (1 case, 1.6%) did not survive at five years after DPC, those with papillary adenocarcinoma (21 cases, 33.33%) had a survival rate of 15.78%, patients with adenocarcinoma tubulopapillary (4 cases, 6.3%) survived in a rate of 66.66%, tubular adenocarcinoma cases (36 patients, 57.1%) had a survival rate of 33.33%, while cases of anaplastic carcinoma did not survive at 5 years (Figure 5).

91.3% of patients with DPC without lymphovascular invasion have survived at 5 years (23 cases, 36.5%), while only 11.9% of cases with lymph-vascular invasion (40 patients, 63.5%) had a survival at 5 years (Figure 6).

Twenty-five patients (39.7%) with D.P.C did not have perineural invasion, with a 5-year survival rate of 82.3%, the remaining 38 patients (60.3%) with perineural invasion presenting a 5-year survival rate of 12.7% (Figure 7).

Multivariate analysis of prognostic factors showed a high risk of death in the presence of lymphovascular invasion ( $p = 0.0031$ ).

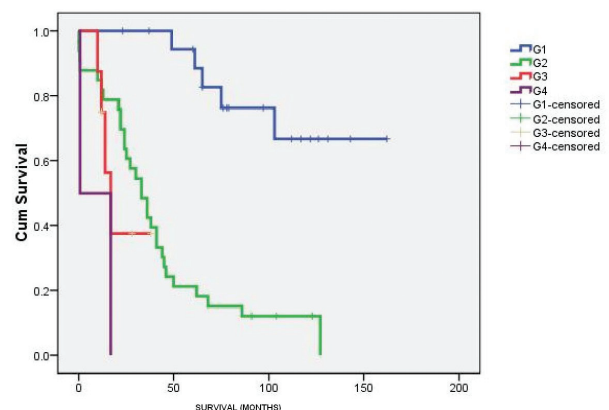


Fig. 4. Survival at 5 years after cephalic pancreatoduodenectomy depending on the degree of G tumor differentiation

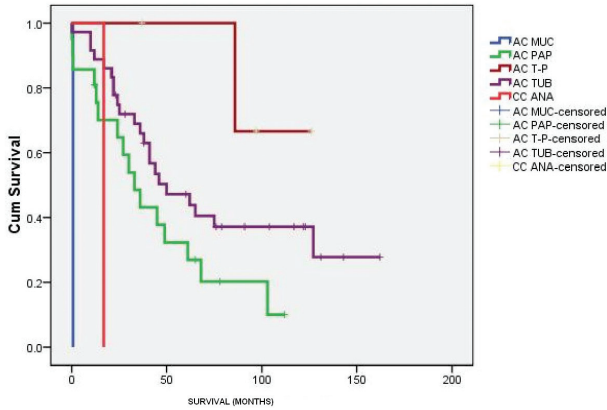


Fig. 5. Survival at 5 years after cephalic pancreatoduodenectomy depending on the type of tumor histopathology

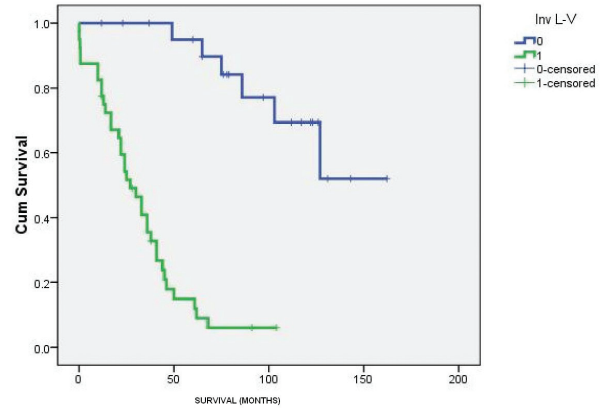


Fig. 6. Survival at 5 years after cephalic pancreatoduodenectomy according to lymph-vascular invasion

**Discussions**

The overall 5-year survival rate for group of 63 patients with DPC from which we obtained data, was 43.1%, with an average survival rate of 69.89 months. Sabater L repor- ted a survival rate at 2 and 5 years of 71% and 53% respectively [1]. Qiao QL and collaborators have found a 5-year survival of 43.3% [2]. Dahl S. and collaborators have reported 40% survival rate at 5 years after 27 Whipple ope- rations performed for ampullary carcinoma between 1995–2005 [3]. Chiche L and colleagues, in a retrospec- tive study on 41 patients with DPC, operated between 1980 and 2003, reported a 5-year survival of 45% [4]. Survival at 5 years after DPC depending on the T pa- rameter showed a 68.3% survival for T1 cases (19 cases, 30.2%), 33.2% for T2 cases (21 patients, 33.3%), 20.4% for T3 cases (17 cases, 27%) and 15.8% for T4 cases (6 patients, 9.5%). Berberat PO and collaborators have found a 50.5% 5-year survival rate for patients in stages T1, T2 5-year survival was 61%, while the patients with T3, T4 did not survive 5 years [5]. Iacono C and colleagues found 16 patients in stages T1–T2, 14 patients in stage T3 and T4 in 29 patients and an overall survival rate at 5 and 10 years of 46% and 33% respectively [6]. Statistical study of

regional lymph nodes invasion shows a 5-year survival rate of 68.3% in cases without regional lymph node invasion (33 cases, 52.4%), respectively, 13.9% for patients with nodal invasion (30 patients, 47.6%).

Park JS and colleagues believe that lymph node meta- stases are the most important risk factor in recurrence after radical resection [8]. Analyzing the group of patients with D.P.C from which we obtained the data about survival (63 patients), we observed that patients with mucinous adenocarcinoma (1 case, 1.6%) did not survive at 5 years, those with papillary adenocarcinoma (21 cases, 33.33%) had a 27% survival rate, patients with tubulo-papillary adenocarcinoma (4 cases, 6.3%) have survived in a per- centage of 90.8%, tubular adenocarcinoma cases (36 pa- tients, 57.1%) had a survival rate of 44.3%, while cases of anaplastic carcinoma showed no survival at 5 years. Given that the ampulla of Vater represents a junction of 4 types of epithelial tissue (ampullary, pancreatic, duodenal, and biliary), we can say that at this level there are tumors of intestinal or pancreatobiliar type. Georgescu SO and col- laborators, in a study of 38 patients with DPC, operated between 1998 and 2007 for periampullary carcinoma, had found 60.5% cases of intestinal-type adenocarcinoma and 39.5% pancreatobiliar type. The survival was signifi- cantly higher in patients with well differentiated tumors, intestinal-type, T1–T2 stages, without regional lymph invasion; following multivariate analysis, the significant prognostic factors were the regional lymph node invasion and the degree of tumor differentiation [9].

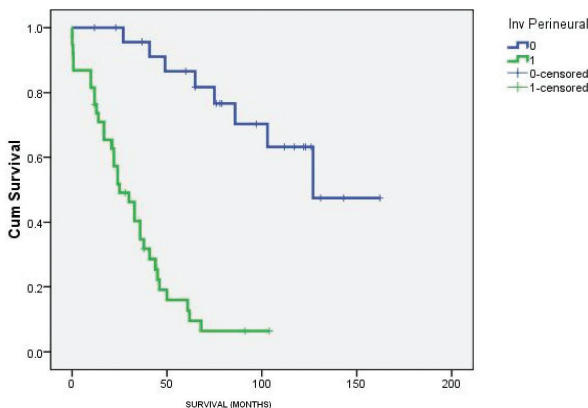


Fig. 7. Survival at 5 years after cephalic pancreatoduodenectomy according to perineural invasion

Regarding lympho-vascular and perineural invasion, in our study, the results of patients with DPC, 91.3% of pa- tients without lympho-vascular invasion survived 5 years (23 cases, 36.5%), while only 11.9% of cases with lym- pho-vascular invasion (40 patients, 63.5%) had survived at 5 years; 25 patients (39.7%) with perineural invasion, had a 5-year survival rate of 82.3%, the remaining 38 pa- tients (60.3%) showing a 5-year survival rate of 12.7%. Van Roest MH and colleagues analyzed 205 patients with periampullary adenocarcinoma, from whom 121 under-

went DPC; perineural invasion was present in 7 of 30 patients with ampullary adenocarcinoma; 5-year survival for the entire group was 32.6%; average survival in cases with perineural invasion was 13.1 months compared with 36 months in cases without invasion [10].

### Conclusions

1. Survival at 5 years after DPC was 43.1%, with an average survival of 69.89 months, which is influenced by tumor extension, regional adenopathies, the histopathological type of tumor, the degree of tumor differentiation and lymphovascular or perineural invasion.
2. The multivariate analysis of prognostic factors shows that the lymphovascular invasion has statistical significance for postoperative survival ( $p = 0.0031$ ).

### References

1. Sabater L, Calvete J, Aparisi L, Cánovas R, Muñoz E, Añón R, et al. – Pancreatic and periampullary tumors: morbidity, mortality, functional results and long-term survival. *Cir Esp* 2009, 86(3): 159–66.
2. Qiao QL, Zhao YG, Ye ML, Yang YM, Zhao JX, Huang YT, Wan YL – Carcinoma of the ampulla of Vater: factors influencing long-term survival of 127 patients with resection. *World J Surg* 2007, 31(1):137–43; discussion 144–6.
3. Dahl S, Bendixen M, Fristrup CW, Mortensen MB – Treatment outcomes for patients with papilla of Vater cancer. *Ugeskr Laeger* 2010, 172(18): 1361–5
4. Chiche L, Alkofer B, Parienti JJ, Rouleau V, Salamé E, Samama G, Segol P – Usefulness of follow-up after pancreatoduodenectomy for carcinoma of the ampulla of Vater. *HPB (Oxford)* 2007, 9(2): 140–5.
5. Berberat PO, Künzli BM, Gulbinas A, Ramanauskas T, Kleeff J, Müller MW, et al. – An audit of outcomes of a series of periampullary carcinomas. *Eur J Surg Oncol* 2009, 35(2): 187–91.
6. Iacono C, Verlatto G, Zamboni G, Scarpa A, Montresor E, Capelli P, et al. – Adenocarcinoma of the ampulla of Vater: T-stage, chromosome 17p allelic loss, and extended pancreaticoduodenectomy are relevant prognostic factors. *J Gastrointest Surg* 2007, 11(5): 578–88.
7. Park JS, Yoon DS, Park YN, Lee WJ, Chi HS, Kim BR – Transduodenal local resection for low-risk group ampulla of vater carcinoma. *Laparosc Adv Surg Tech A* 2007, 17(6): 737–42.
8. Georgescu SO, Neacșu CN, Vintilă D, Popa P, Florea N, Mihailovici MS – The histopathologic type of the periampullary tumors. Is it important for survival? *Chirurgia* 2009,104(6): 697–700.
9. van Roest MH, Gouw AS, Peeters PM, Porte RJ, Slooff MJ, Fidler V, de Jong KP – Results of pancreaticoduodenectomy in patients with periampullary adenocarcinoma: perineural growth more important prognostic factor than tumor localization. *Ann Surg* 2008, 248(1): 97–103. Comment in: *Ann Surg* 2009, 249(3): 545.