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Original article

Duodenal Adenocarcinoma: Surgical Results of 27 Patients Treated at a Single Center[☆]

Josefina López-Domínguez,[a] Juli Busquets,[a,] Lluis Secanella,[a] Nuria Peláez,[a] Teresa Serrano,[b] Juan Fabregat[a]*

[a] *Unidad de Cirugía Hepatobiliar y Pancreática, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*
[b] *Servicio de Anatomía Patológica, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*

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ABSTRACT

Introduction: Duodenal adenocarcinoma is a rare malignancy. Given the rarity of the disease, there is limited data related to resection results. The objective is to analyze results at our hospital after the curative resection of duodenal adenocarcinoma (DA).

Material and methods: The variables were retrospectively collected from patients operated on between 1990 and 2017 at our hospital.

Results: A total of 27 patients were treated. Twenty-three patients (85%) underwent pancreaticoduodenectomy, and 4 patients (15%) with tumors located in the third and fourth portions of the duodenum underwent segmental duodenal resection. The overall postoperative morbidity was 63% (17 patients). Postoperative mortality was 7% (2 patients); however, postoperative mortality related to surgery was 4% (1 patient). All patients had negative resection margins. A median of 18 lymph nodes (range, 0–38) were retrieved and evaluated, with a median of 1 involved node (range, 0–8). Median follow up was 23 (9–69.7) months. Actuarial overall survival was 62.2 (25.2–99.1) months. Actuarial disease-free survival was 49 (0–133) months.

Conclusions: The surgical treatment of duodenal adenocarcinoma is associated with a high morbidity, although it achieves considerable survival. Depending on the tumor location and if there is no pancreatic infiltration, segmental duodenal resection with negative margins is an alternative to cephalic pancreaticoduodenectomy.

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Adenocarcinoma duodenal: resultados del tratamiento quirúrgico de una serie unicéntrica de 27 pacientes

RESUMEN

Introducción: El adenocarcinoma de duodeno es una neoplasia poco frecuente, sobre la que existen pocas experiencias publicadas de los resultados tras su resección. El objetivo es analizar los resultados obtenidos en nuestro centro tras la resección curativa del adenocarcinoma duodenal (AD).

Material y métodos: Estudio retrospectivo de los pacientes intervenidos con resección cura-
tiva por AD entre 1990 y 2017 en nuestro hospital.

Resultados: Se intervinieron 27 pacientes. En 23 casos (85%) se realizó duodenopancreatec-
tomía cefálica (DPC) y en 4 casos (15%) con localización en 3ª-4ª porción duodenal se realizó
duodenectomía segmentaria (DD). La morbilidad postoperatoria global fue del 63% (17
pacientes). La mortalidad postoperatoria global fue 7% (2 pacientes), sin embargo, la
mortalidad postoperatoria relacionada con la cirugía fue de 4% (1 paciente). El estudio
anatomopatológico evidenció resección con márgenes libres en todos los casos interveni-
dos. La mediana de adenopatías resecadas fue 18 (0 a 38), siendo 1 (0 a 8) las adenopatías
afectas. Tras una mediana de seguimiento de 23 (9–69,7) meses, la supervivencia actuarial
fue de 62,2 (25,2 a 99,1) meses y la supervivencia actuarial libre de enfermedad fue de 49 (0 a
133) meses.

Conclusiones: La resección quirúrgica del adenocarcinoma duodenal comporta una elevada
morbilidad postoperatoria, sin embargo, consigue una supervivencia prolongada. Depen-
diendo de la localización y en ausencia de infiltración pancreática, la duodenectomía
segmentaria con márgenes libres es una alternativa a la duodenopancreatectomía cefálica.

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Introduction

Duodenal adenocarcinoma (DA) is an uncommon neoplasm,
even though the duodenum is the most common location for
adenocarcinomas of the small intestine.[1–4] The majority of DA
are located in the second part of the duodenum (D2), followed
by the 3rd and 4th parts (D3-D4), while the first part is very
rarely affected.[3] The symptoms are nonspecific, such as
abdominal pain, nausea, vomiting, asthenia or weight loss,
and abdominal pain is the most frequent. In cases of advanced
disease, jaundice, intestinal obstruction or anemia may occur.
Due to the non-specificity of the symptoms, the diagnosis of
the disease is usually late.

The suspected diagnosis is confirmed by upper gastroin-
testinal endoscopy with biopsy. Multislice abdominal compu-
ted tomography scan is essential for the extension study.[5] The
treatment of choice is surgical resection. Regarding the
technique, initially pancreaticoduodenectomy (PD) was con-
sidered standard treatment.[6] Afterwards, segmental resection
or surgical duodenectomy was considered a valid option for
this type of tumors, (DD), depending on the location, resection
margins, surgical lymphadenectomy.[4,7–9] However, there is no
consensus in this regard, some authors support PD|as, the
technique of choice in all cases.[10,11] The objective of this study
is to analyze the results obtained at our hospital after the
curative resection of DA using PD, DD.

Methods

Between 1990 and 2017, we retrospectively registered patients
who underwent surgery with curative intent for DA at the
Hospital Universitari de Bellvitge (Barcelona, Spain). Demo-
graphic, clinical, surgical and pathological variables were
collected, as well as data regarding the postoperative and long-
term evolution. The inclusion period ended in March 2017. The
patients were monitored in outpatient surgery consultations,
and follow-up was completed in March 2018.

Preoperative Study

All patients were studied using upper gastrointestinal endos-
copy with biopsy and computed tomography. The presence of
distant metastases and arterial invasion (superior mesenteric
artery, hepatic artery or celiac trunk) were defined as
unresectable criteria. Regarding venous involvement, no
resections were performed in patients with large duodenal
tumors that would involve obliteration of the superior
mesenteric vein. Neither advanced patient age nor tumor
size were contraindications for surgery.

Surgical Technique and Pathological Study

The surgical techniques used were PD in those cases in which
the tumor affected D2 or there was invasion of the pancreas,
and DD for patients with D3-D4 involvement. In tumors that
were treated with PD due to their location, standard locore-
gional lymphadenectomy was performed (peripancreatic
lymphadenopathies, hepatic hilum and right margin of the
superior mesenteric artery). The pathological study analyzed
the degree of tumor differentiation, tumor size, involvement of
resection margins, number of affected and resected lympha-
denopathies and established the TNM stage (7th Edition of the
American Joint Committee on Cancer [AJCC] Staging system for
small bowel adenocarcinoma[12]). In both the DD and PD, the
intestinal margin was considered a resection margin. The
lymph node ratio was defined as the number of lymph nodes
affected over the total number of resected lymph nodes.

Postoperative Morbidity

Postoperative morbidity was registered in accordance with the
Clavien-Dindo classification.[13] Postoperative mortality was

defined as death that occurred during hospitalization or up to 90 days after surgery. Delayed gastric emptying (DGE) was defined as the inability to tolerate oral intake after the first postoperative week, following the definition of the International Study Group of Pancreatic Surgery (ISGPS).[14] Pancreatic fistula was defined as discharge of fluid through the drain tubes that was rich in amylase (amylase ×3 compared to normal blood levels) after postoperative day 3, applying the ISGPS classification.[15] All patients were followed by a member of the surgical team after hospital discharge.

Statistical Analysis

The Stata v.13® statistical package was used. Initially, a descriptive analysis of the series was performed using measures of central tendency (median) and dispersion (interquartile range and range) for quantitative variables. Next, the series was divided into 2 study groups according to the technique used, PD and DD, and the 2 groups were compared using Fisher's test for qualitative variables and the Mann–Whitney U for quantitative variables. A P level <.05 was considered statistically significant. Actuarial survival rates (global and disease-free) were calculated for each study group using the Kaplan–Meier test. A study of risk factors for mortality and recurrence was conducted with univariate Cox regression models. For the multivariate analysis, we selected the significant variables from the univariate study, the study variable (surgical technique), as well as the demographic variables (age and sex).

Results

During the study period, 27 patients were treated surgically. In 23 cases (85%), PD was conducted, and in 4 cases (15%) DD was performed (Table 1). The median patient age was 63.4 (50.8–74.1)

Table 1 – Duodenal Adenocarcinoma: Results of Surgical Treatment, Details of Surgical Technique and Postoperative Morbidity.

N	Age	Sex	Surgical Technique	Morbidity	Clavien-Dindo	Postoperative Hospital Stay
1	74	M	PD	DGE, pancreatic fistula(B), SSI	II	21
2	45	F	PD	Pancreatic fistula(A)	II	29
3	68	M	PD	Pancreatic fistula(B), hemorrhage, SSI	IIIa	64
4	82	F	DD	Infectious complications (SSI, respiratory, urinary, intra-abdominal collection), exitus	V	40
5	75	M	PD	Pancreatic fistula(A), intra-abdominal collection	IIIa	7
6	61	F	PD	DGE, pancreatic fistula(B), Intra-abdominal collection	IIIa	37
7	46	M	DD	DGE, intra-abdominal collection	II	8
8	74	F	PD	————	II	15
9	63	F	PD	————	II	9
10	43	M	PD	————	II	11
11	74	F	DD	————	I	7
12	76	F	PD	————	II	22
13	51	M	DD	DGE, intra-abdominal collection	IIIa	47
14	30	M	PD	DGE, intra-abdominal collection	IIIa	28
15	65	M	PD	Pancreatic fistula(B), intra-abdominal collection	IIIa	29
16	83	M	PD	Pancreatic fistula(B), SSI, intra-abdominal collection	IIIa	30
17	42	F	PD	————	I	14
18	69	M	PD	G-J dehiscence, re-operation, exitus	V	6
19	37	F	PD	DGE	II	36
20	50	M	PD	DGE	II	24
21	63	M	PD	UTI	II	19
22	60	M	PD	DGE	II	23
23	50	F	PD	DGE	II	24
24	67	F	PD	DGE, SSI	II	25
25	63	F	PD	————	I	11
26	65	M	PD	————	I	20
27	60	F	PD	————	I	9

DD: duodenectomy; PD: pancreaticoduodenectomy; F: female; SSI: surgical site infection; UTI: urinary tract infection; M: male; DGE: delayed gastric emptying.
Morbidity according to Clavien-Dindo classification[30]; hospital stay in days.

years, with no significant differences between the 2 groups. The patients included 13 women (48%): 11 in the PD group (48%) and 2 in the DD group (50%).

Postoperative Results

The overall postoperative morbidity was 63% (17 patients). Three patients (11%) presented a complication higher than IIIa of the Clavien–Dindo classification.[13] When we analyzed the complications in terms of the technique performed, postoperative morbidity was 65% after PD (15 out of 23 patients) and 75% after DD (3 out of 4 patients), with no statistically significant differences (Table 2). The most frequent complication in the entire series was DGE, which was observed in 37% (10 patients), with no statistically significant differences between the two techniques. Septic complications were seen in 44% (12 patients). Finally, the pancreatic fistula rate after PD was 30% (7 patients: 2 type A and 5 type B). The median postoperative stay was 22 (11–29) days, which was similar in both groups. Out of the total of the series, one patient (4%) had to be reoperated due to dehiscence of the gastrojejunal anastomosis, requiring sutures and surgical drain placement. Postoperative

mortality was 7% (2 patients). One patient of the PD group died due to multiple organ failure after being reoperated for anastomotic dehiscence. Another patient of the DD group died 40 days after surgery due to hyperammonemic encephalopathy and respiratory failure, without having presented any intra-abdominal complications. There were no statistically significant differences in postoperative mortality between the two study groups (P = .279) (Table 2).

Pathological Study

The pathological study showed that the majority of patients were pT4 (15 patients, 55%), with pN1 lymph node involvement (15 patients, 55%) according to the TNM classification (7th edition of the AJCC[12]) (Tables 3 and 4) (Fig. 1). In 4 patients, the pathological study could not be fully recovered. The degree of tumor differentiation most frequently registered was moderately differentiated (41%). Tumor size was greater than 30 mm in 59% (16 cases). In all cases, resection was performed with free margins. The median number of resected lymphadenopathies was 18 (0–38), including 22 in the PD group (4–38) and 12.5 (0–15) in the DD group, which were statistically significant differences (P = .016).

Table 2 – .Postoperative Morbidity: Comparison Between the 2 Study Groups.

Variables	Total (n = 27)	PD (n = 23; 85%)	DD (n = 4; 15%)	P Value
Complications, n (%)	18 (67%)	15 (65)	3 (75%)	.702
DGE, n (%)	10 (37)	8 (35)	2 (50)	.613
PF, n (%)		7 (30)		
Hemorrhage, n (%)	1 (4)	1 (4)	0	1
Infectious, n (%)	12 (44)	9 (31)	3 (75)	.294
Incisional, n (%)	5 (18)	4 (17)	1 (25)	1
Respiratory, n (%)	1 (4)	0	1 (25)	.148
Urinary, n (%)	2 (7)	1 (5)	1 (25)	.279
Catheter, n (%)	1 (4)	0	1 (25)	.148
IA abscess, n (%)	8 (30)	5 (22)	3 (75)	.065
Re-operation, n (%)	1 (4)	1 (4)	0	1
Postoperative death, n (%)	2 (7)	1 (4)	1 (25)	.279

DD: duodenectomy; PD: pancreaticoduodenectomy; IA: intra-abdominal; PF: pancreatic fistula; DGE: delayed gastric emptying.

Table 3 – Pathologic Anatomy Results.

		Total (n = 27)	PD (n = 23; 85%)	DD (n = 4; 15%)
TNM				
T	pT1	1 (4%)	1 (4%)	0 (0%)
	pT2	2 (7%)	2 (9%)	0 (0%)
	pT3	9 (33%)	6 (26%)	3 (75%)
	pT4	15 (55%)	14 (61%)	1 (25%)
N	pN0	9 (33%)	6 (26%)	3 (75%)
	pN1	15 (55%)	14 (61%)	1 (25%)
	pN2	3 (11%)	3 (13%)	0 (0%)
Tumor differentiation grade				
Well-differentiated		3 (11%)	2 (9%)	1 (25%)
Moderately-differentiated		11 (41%)	10 (43%)	1 (25%)
Undifferentiated		9 (33%)	8 (35%)	1 (25%)
Not registered		4 (15%)	3 (13%)	1 (25%)
Lymphadenopathies				
Resected (median, range)		18 (0 to 38)	22 (4 to 38)	12.5 (0 to 15)
Affected (median, range)		1 (0 to 8)	2 (0 to 8)	0 (0 to 1)
Ratio (median, range)		8.83 (0 to 43.8)	9.1 (0 to 43.8)	0 (0 to 7.7)
Involved surgical margins		0 (0%)	0 (0%)	0 (0%)

NR	Surgical Technique	Differentiation Grade	TNM	Tumor Size (mm)	Affected/ resected LA	Recurrence	DFS (Months)	Survival (Months)	Current State
									Table 4 – Duodenal Adenocarcinoma: Surgical Treatment Results, Pathology Study and Long-term Evolution.
1	PD	Moderate	pT4N2	30	4/35	No	9.1	9.1	Living
2	PD	Moderate	pT4N1	35	2/20	Yes	20.3	20.8	Living
3	PD	Well-diff.	pT3N0	48	0/12	No	23.6	23.6	Living
4	DD	Not registered	pT3N0	65		–		1.3	Exitus (post-op)
5	PD	Undifferentiated	pT4N2	60	4/17	Yes	15.8	17.7	Living
6	PD	Well-diff.	pT3N1	20	1/24	No	42.9	42.9	Living
7	DD	Moderate	pT3N0	30	0/15	No	46.9	46.9	Living
8	PD	Moderate	pT4N2	70	7/26	Yes	5.6	10.1	Exitus
9	PD	Undifferentiated	pT2N1	45	1/ 4	No	66.2	66.2	Exitus
10	PD	Not registered	pT3N1	25	2/22	No	58.1	58.1	Exitus
11	DD	Well-diff.	pT4N0	6	0/12	No	70.7	70.7	Living
12	PD	Undifferentiated	pT3N1	40	3/26	Yes	3.06	3.4	Exitus
13	DD	Undifferentiated	pT3N1	70	1/13	No	92.9	92.9	Living
14	PD	Undifferentiated	pT4N1	80	3/35	Yes	11.9	35.5	Exitus
15	PD	Undifferentiated	pT1N0	25	0/18	No	99.6	99.6	Living
16	PD	Moderate	pT4N0	28	0/17	No	94.3	94.3	Exitus
17	PD	Moderate	pT3N0	40	0/29	No	124.9	124.9	Living
18	PD	Moderate	pT4N1	25	7/16	–		0.2	Exitus (post-op)
19	PD	Undifferentiated	pT4N1	40	1/12	Yes	123.4	180.4	Living
20	PD	Moderate	pT4N1	50	8/26	Yes	13.7	16.4	Exitus
21	PD	Moderate	pT4N1	30	5/38	Yes	10.6	13	Exitus
22	PD	Undifferentiated	pT4N1	70	2/22	Yes	3.7	7.5	Exitus
23	PD	Undifferentiated	pT4N1	45	3/15	Yes	4	5.06	Exitus
24	PD	Moderate	pT3N1	55	2/27	Yes	50.6	63.1	Exitus
25	PD	Moderate	pT4N0	8	0/14	No	239.5	239.5	Living
26	PD	Not registered	pT4N1			Yes	4.6	5.1	Exitus
27	PD	Not registered	pT2N0	12		Not registered	12.4	13.2	Exitus

Well-diff.: well-differentiated; DD: duodenectomy; PD: pancreaticoduodenectomy; DFS: disease-free survival, LA: lymphadenopathies.

Survival and Follow-up

The median follow-up was 23 (9–69.7) months. During this period, 15 (55%) patients died (14 PD and 1 DD) and 12 (44%) patients were alive (9 PD and 3 DD). The overall 1, 3 and 5-year survival rates in PD were 74, 54 and 47%, respectively. In DD, the 1, 3 and 5-years rates were all 75%. No statistically significant differences were found between the two techniques (Fig. 2).

The median overall survival was 62.2 (25.2–99.1) months. Out of all the variables analyzed in the univariate study, only the lymph node ratio greater than 0.20 was a risk factor for long-term mortality ($P = .009$), a result that was confirmed by the multivariate analysis (Table 5).

Out of the total series, 13 patients (48%) had recurrence, 10 of whom died and 3 are still alive. All these patients had been treated by PD. The 1, 3 and 5-year disease-free actuarial survival rates were 71, 55 and 49%, respectively. The median disease-free survival was 49 (0–133) months (Table 4). None of the variables analyzed was a risk factor for long-term recurrence in the univariate or multivariate study.

Discussion

There are few publications in the literature analyzing the surgical results of DA.[16] The choice of surgical technique (PD vs. DD) is based on the location of the tumor and the presence
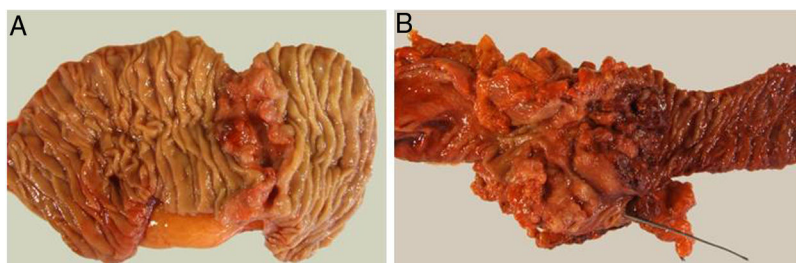

Fig. 1 – Pathological study of the surgical resection specimens after duodenectomy (A) and pancreaticoduodenectomy (B).
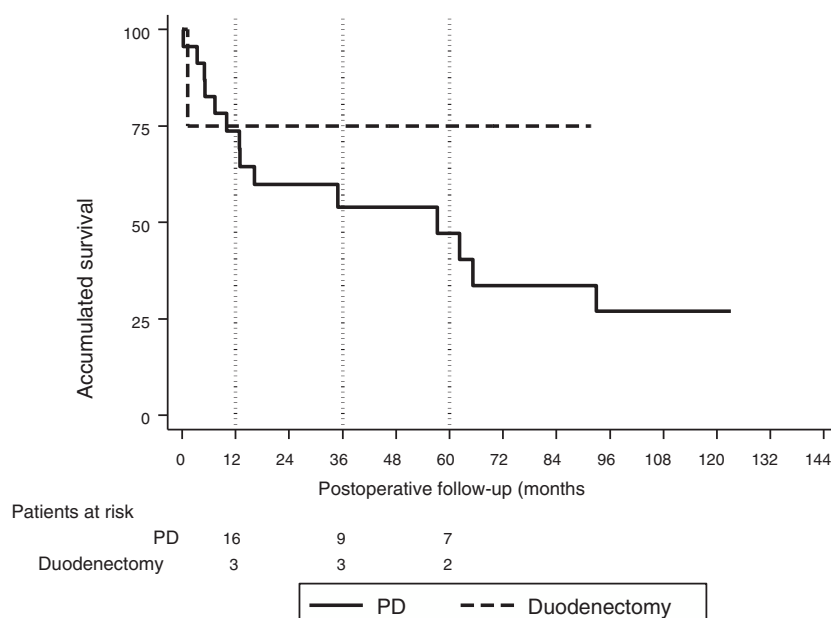
Fig. 2 – Survival after resection for duodenal adenocarcinoma, Kaplan–Meier analysis (log-rank, P = .327). Dashed line: duodenectomy group results. Solid line: pancreaticoduodenectomy group results (Hospital Universitari de Bellvitge. 1990–2017).

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Table 5 – Study of Risk Factors for Long-term Mortality After Surgery for Duodenal Adenocarcinoma (Hospital Universitari de Bellvitge, 1990–2017).

Variable	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	P
Duodenectomy surgical technique	0.38 (0.05 to 2.88)	.346	0.52 (0.06 to 4.28)	.542
Age > 70	1.37 (0.43 to 4.33)	.589	1.91 (0.31 to 11.9)	.485
Females	0.81 (0.29 to 2.25)	.683	1.16 (0.31 to 4.44)	.824
ASA classification		.653		
ASA II	0.64 (0.16 to 2.47)	.514		
ASA III	1.22 (0.39 to 3.88)	.731		
Transfusion of more than 1 unit of packed red blood cells during post-op (first 48)	1.45 (0.49 to 4.32)	.502		
Presence of post-op complications	0.88 (0.31 to 2.50)	.813		
Tumor size greater than 30 mm	1.70 (0.58 to 5.00)	.337		
Tumor grade differentiation				
G2	0.74 (0.21 to 2.70)	.654		
G3	0.73 (.19 to 2.78)	.643		
Lymph node ratio N > 0.20	4.23 (1.44 to 12.4)	.009	4.87 (1.08 to 21.9)	.039

ASA: American Society of Anesthesiologists; CI: confidence interval; HR: hazard ratio.

of pancreatic infiltration. Classically, the technique of choice for DA was PD[6] because it was considered the only method that could offer acceptable cancer outcomes. Subsequently, publications emerged with comparable results in terms of survival for DD and PD.[4,17,18] Even so, there is still controversy about which oncological approach is the most appropriate, and there are authors who currently defend PD as the best treatment.[11] In our experience, morbidity after resection for DA is 65% in the PD group and 75% in the DD group, with no statistically significant differences, which are results similar to other authors.[4,19] However, several groups[19,20] defend DD as a technique with similar postoperative morbidity. The post-operative mortality in our series was 7%, which is similar to

publications by others.[1,4,19,21–23] Like our results, other authors have compared postoperative mortality between PD and DD, finding no statistically significant differences.[4,19] Postoperative mortality in our DD group due to adenocarcinoma was high (1 out of 4 patients); however, the cause of death of the patient in this group was not related to the surgical technique. When we reviewed our experience in DD for different indications, we have found a lower mortality rate (4%).[24,25]

Several prognostic factors have been proven to influence DA survival. Some of them refer to patient age,[23,26] sex,[27] tumor differentiation[10,26] and tumor stage.[26] In the pathological study, the variables related with the prognosis of DA, so far, are the involvement of the resection margin,[1,4,10,18,21] number of

resected lymphadenopathies, involvement of resected lymphadenopathies and the lymph node ratio.[4,7,21,22,26,28,29] In our series, the involvement of the resection margin was zero in both study groups, with an actuarial 5-year survival after resection of 52%. Several authors have demonstrated that survival is affected if there is involvement of the resection margins. For instance, Sohn et al.[10] published a 5-year survival rate of 58% in the case of R0 and 0% in the case of R1. Similar values are described by Poultsides et al.[21] with a 5-year survival of 55% in R0 and 0% in R1.

The importance of lymphadenectomy is also well documented in the literature, despite there being no consensus on the number of nodes to resect.[4,7,21,22,26] The AJCC recommends resecting a minimum of 6 nodes in DA surgery, although there are authors who believe that this number should be greater for better staging.[3,21,28] Sarela et al.[23] found statistically significant differences in 5-year survival between pN0 and pN+ patients when the number of resected nodes was equal to or greater than 15. In contrast, if the number of resected nodes was less than 15, the 5-year survival results were similar between both groups. In our study, we registered a greater number of nodes after PD compared to DD (22 vs. 12.5; P = .016), although this did not imply better survival. Other authors demonstrated similar results to our experience. Sakamoto et al.[11] published a series with an average of 26 resected lymph nodes in the PD group vs. 14 nodes in the DD group (P = .001), with no differences in survival between the two groups. Along the same lines, Cloyd et al.[26] showed results of a lymphadenectomy with a greater number of lymph nodes in the PD compared to DD (11 ± 8.9 vs. 6.8 ± 7.8; P < .0001), with no changes in long-term survival between the two groups. Several authors have shown that the lymph node ratio (affected nodes/resected nodes) is the most appropriate prognostic predictor.[21,26,28,29] In our series, the lymph node ratio was the only variable that was proven to be a prognostic factor for long-term mortality. Finally, we have not observed differences in survival when comparing the 2 surgical techniques (PD and DD).[4,11,26] In our series, the overall survival after resection for DA was 62.2 months and 52% after 5. These results are slightly higher than other published reports, with a survival between 30–45 months[4,19,22,27] and a 5-year survival of 23%–48%.[1,4,19,21,22]

Being a rare entity, the number of patients in our study is low, despite a prolonged period of study. Therefore, it is difficult to draw conclusions, which is one of the limitations of this study. However, after analyzing our experience and that of other authors, we believe that both surgical options can be considered, depending on the tumor location and the degree of pancreatic involvement.

Conclusion

Surgical resection of DA involves high postoperative morbidity, even though it is able to prolong survival. Depending on the location and in the absence of pancreatic invasion, segmental DD with free margins is an alternative to PD.

Conflict of Interests

The authors have no conflict of interests to declare.

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