Comparative study of the radical and standard lymphadenectomy in the surgical treatment of adenocarcinoma of the ampula of Vater

Estudo da linfadenectomia radical comparada à linfadenectomia standard no tratamento cirúrgico do adenocarcinoma da papila de Vater

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A B S T R A C T

Objective: To evaluate surgical morbidity and mortality in patients undergoing gastropancreatoduodenectomy (GPD) and standard or radical lymphadenectomy for adenocarcinoma of the papilla, analyzing prognostic factors regarding overall and disease free survival. Methods: We retrospectively analyzed the period from 1999 to 2007 at the Department of Abdominopelvic Surgery of INCA-RJ, during which there were 50 cases of GPD for adenocarcinoma of the duodenal papilla. They were divided in two groups according to lymphadenectomy (group A: standard lymphadenectomy; and group B: radical lymphadenectomy). Results: The median of age was similar in both groups, as well as the distribution between sexes. In the comparison between lymphadenectomies only the number of resected lymph nodes (group A: 12.3 and group B: 26.5) and operative time (group A 421 minutes and group B 474) were significantly different. There were no statistically significant differences in the two groups regarding operative mortality and morbidity and hospitalization time. The disease-free survival (group A 35 months and group B 51) and overall survival (group A 38 months and group B 53) were higher in the radical lymphadenectomy group, but were not statistically significant. There were no cases of metastatic lymph nodes to other groups without concomitant involvement of the pancreato-duodenal lymph node chains (13, 17), suggesting a pattern of lymph node spread. Conclusion: Despite the radical lymphadenectomy present higher rates of disease-free survival and overall survival, such data were not statistically significant. Further studies should be conducted to assess the actual role of lymphadenectomy in adenocarcinoma of the duodenal papilla.

Key words: adenocarcinoma, duodenal papilla, lymphadenectomy, gastropancreatoduodenectomy.

INTRODUCTION

The role of lymphadenectomy for periampullary tumors remains controversial, especially with regard to adenocarcinoma of the papilla. The number of lymph nodes examined after curative surgery has been shown to be very important in identifying the extent of disease. Some articles report an increase in the rate of survival with an increase in lymph node evaluation, such as in gastric [1-4], cólon[5-8] and breast[9,10] cancers.

Extended lymphadenectomy in patients with adenocarcinoma of the duodenal papilla increases surgical time, but not morbidity and mortality, as well as in hospital length of stay[11]. However, the therapeutic benefit of the performance of a wider node dissection in patients with periampullary adenocarcinoma remains unclear, as does the increase in the staging accuracy[12].

This study aims to evaluate the surgical morbidity and mortality in patients undergoing gastroduode nopancreatectomy (GPD) with standard and radical lymphadenectomy for adenocarcinoma of the papilla, comparing the prognostic factors with overall and disease free survival.

METHODS

We selected 50 consecutive patients referred to the National Cancer Institute (INCA), between January 1999 and December 2007 for surgical treatment of gastroduodenpancreatectomia for adenocarcinoma of papilla of Vater for retrospective analysis.

Based on the Japanese classification by nodal group[13] (Figures 1 and 2) the patients were divided in two

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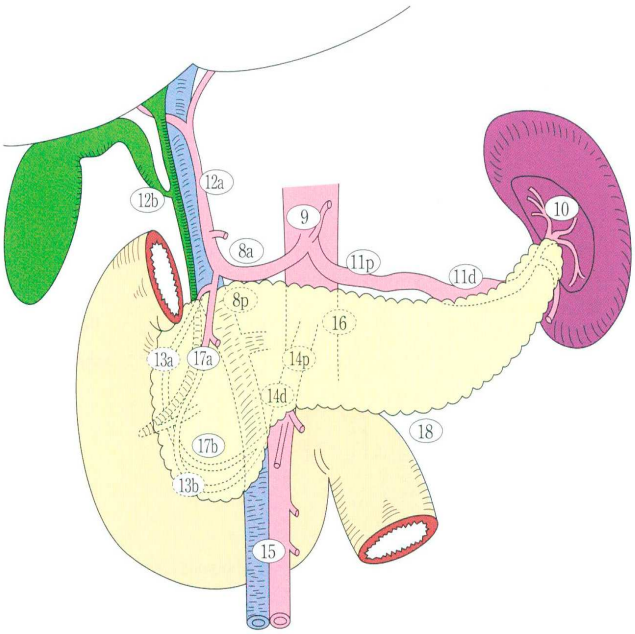

Figure 1 - *Peri-pancreatic lymph nodes. Biliary Tract Carcinoma Classification (2001).Japanese Society of Biliary Surgery (JSBS)[13].*

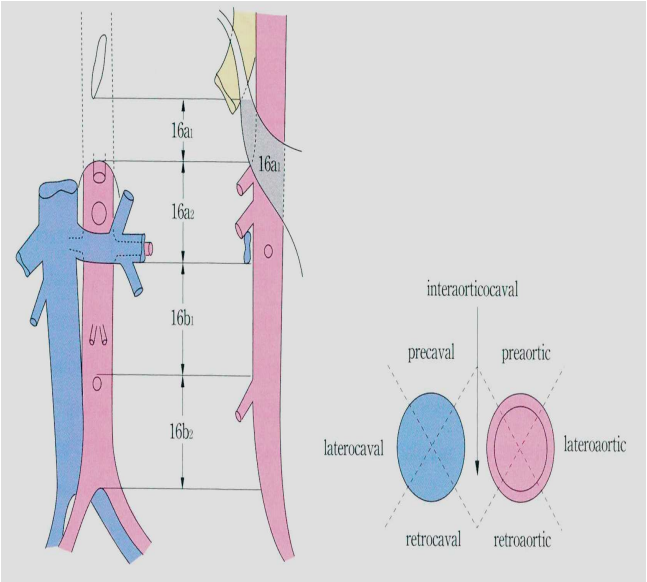

Figure 2 - *Para-aortic lymph nodes dissection (16). Biliary Tract Carcinoma Classification (2001). Japanese Society of Biliary Surgery (JSBS)[13].*

groups according to the extent of lymphadenectomy. Group A: GPD with standard lymphadenectomy (default), resecting the lymph nodes of groups of the lesser and greater gastric curvature (groups 3 and 4), lymph nodes above and below the pylorus (groups 5 and 6), pancreatoduoenal (groups 17 e 13) and along the superior mesenteric vein (group 14v). Group B: GPD with radical lymphadenectomy, where resection followed the same technique of standard resection plus hepatic artery nodes (group 8), celiac trunk (group 9), hepato-duodenal ligament (group 12), lateral border of the superior mesenteric artery (14th group) and the para-aortic lymph nodes of the right renal vein to the inferior mesenteric artery (group 16a2 and 16b1).

All patients underwent a classic GPD without pylorus preservation and had confirmation, by pathological anatomy in the surgical specimen, of adenocarcinoma of the papilla of Vater, in studies performed by a single group of pathologists at the National Cancer Institute.

Were analyzed the following variables in the two groups: demographics, more frequent symptoms, duration, preoperative biliary drainage, surgical time, blood transfusion, type of pancreatic anastomosis, histological type of primary tumor, number of removed lymph nodes, lymph node involvement by group, stage, surgical morbidity and mortality, hospitalization, disease-free survival and overall survival. Survival was calculated by the Kaplan-Meier curves and compared by log rank test, the significance of all statistical tests set at $p<0.05$.

RESULTS

We evaluated 50 patients undergoing GPD in the National Cancer Institute (INCA-RJ) between January 1999 and December 2007; 29 of these were enrolled to group A - standard lymphadenectomy, and 21 to group B - radical lymphadenectomy.

The medians of age for both groups were similar (group A: 57 years and group B: 59.7), as well as the distribution by race. The time of presentation of symptoms was also approximately the same between groups (group A: 96, five days and group B: 100, three days); the chief complaint was jaundice, occurring in group A in 44% of cases and in group B in 61.9%.

Regarding surgery, we found the following values: Group A mean operative time was 421min, the operative morbidity was 51.7% (Table 1), pancreatic fistula was the most prevalent surgical complication occurring in five patients, surgical mortality was 10.3% and the number of lymph nodes resected was 12.3. In group B the average time of surgery was 474min, operative morbidity was 42.8% (Table 1), pancreatic fistula was the most prevalent surgical complication occurring in three patients, operative mortality was 4.7% and the number of lymph nodes resected was 26.5, but only the operative time and mean resected lymph nodes were statistically significant (p=0.02). In this study there were no cases of metastatic lymph nodes to other nodal groups without involvement of pancreato-duodenal lymph node chains (13,17), suggesting a pattern of lymph node spread (Table 2).

None of the prognostic factors studied that were related with poor survival for adenocarcinoma of the papilla in the literature achieved statistical significance in this study (Table 3).

The disease-free survival (Figure 3) and overall survival (Figure 4) were better in the group of radical lymphadenectomy, but without statistical significance.

DISCUSSION

This study aimed to evaluate the role of lymphadenectomy in patients with resectable adenocarcinoma of the duodenal papilla and without distant metastases through a comparative analysis of variables related to surgical procedure itself and its interference in the evolutionary course of the disease.

GPD remains the best treatment for adenocarcinoma of the duodenal papilla. Despite the fall in its mortality rate, its morbidity remains high, the

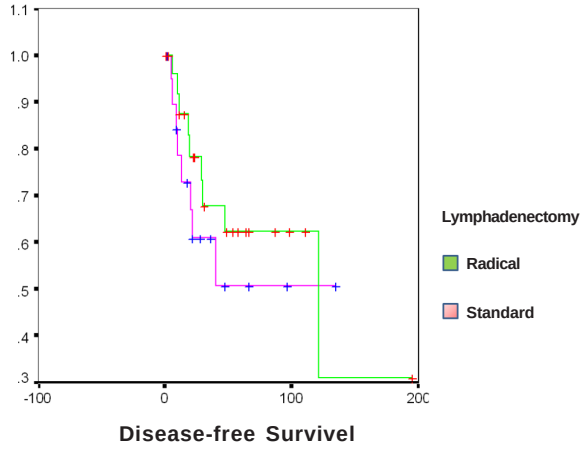

Figure 3 - *Curve of disease-free survival of standard and radical lymphadenectomy.*

Table 1 – Comparison of surgical morbidity and mortality after gastroduodenopancreatectomy with standard and radical lymphadenectomy.

Complications	Standard Lymphadenectomy	Radical Lymphadenectomy Patients (%)
Overall Morbidity	15 (51,7%)	9 (42,8%)
Surgical Complications		
Pancreatic fistula	5 (17,2%)	3 (14,2%)
Gastroparesia	4 (13,8%)	2 (9,5%)
Bleeding abdominal	2 (6,9%)	1 (4,8%)
Biliary fistula	1 (3,4%)	0 (0%)
Gastrointestinal fistula	0 (3,4%)	1 (4,8%)
Wound infection	1 (3,4%)	1 (4,8%)
Overall Complications	1 (3,4%)	1 (4,8%)
Pulmonary embolism	1 (3,4%)	0 (0%)
Pneumonia		
Death		

Table 2 - Lymph node groups involved.

Lymph Node Group	Standard Lymphadenectomy (group A)	Radical Lymphadenectomy (group B)
Group 17	8 patients (27,6%)7 patients (33%)	
Group 13	6 patients (20,7%)	7 patients (33%)
Group 12	0 patients (0%)	0 patients (0%)
Group 14	2 patients (6,9%)	2 patients (9,5%)
Group 9	0 patients (0%)	0 patients (0%)
Group 8	0 patients (0%)	2 patients (9,5%)
Group 16	0 patients (0%)	1 patients (4,8%)
Group 3	0 patients (0%)	0 patients (0%)
Group 4	0 patients (0%)	0 patients (0%)
Group 5	0 patients (0%)	0 patients (0%)
Group 6	0 patients (0%)	0 patients (0%)

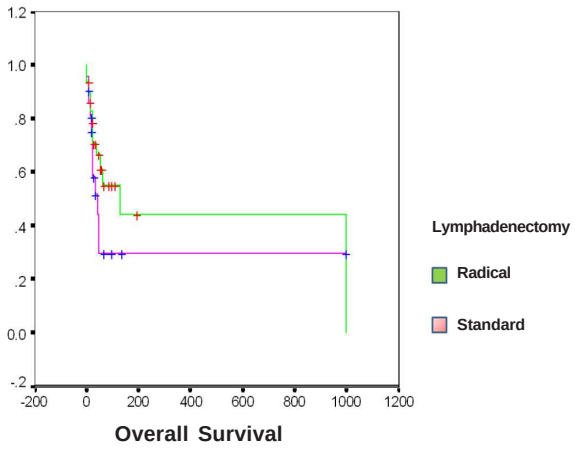

Figure 4 - *Curve of overall survival of standard and radical lymphadenectomy.*

pancreatic fistula being the most important. Talamini et al.[14] reported an overall survival at five years of 38% with an operative mortality of 3.8% and a surgical morbidity of 47%, the pancreatic fistula being most common complication, occurring in 25% of cases. In our study we found no statistically significant differences regarding the length of hospitalization, morbidity and mortality rate, disease-free and overall survival for both standard and radical lymphadenectomies, those values being consistent with the literature, as described above.

Nodal involvement is the most important independent prognostic factor in patients with adenocarcinoma of the papilla[15-21], followed by the depth of tumor infiltration[15-17,22], negative margins[16,23], histological grade[22] and the need for blood transfusion[18,22].

O' Connell et al.[24] described an overall survival for patients with positive and negative lymph nodes of 21.9% and 54.1%, respectively. Recently, Sakata et al.[25] examined the impact of nodal disease on survival of 62 patients with adenocarcinoma of the papilla, finding an overall survival at five years of 89% in cases without lymph node involvement, 48% in cases of involvement of one to three lymph nodes and 0% in cases of metastasis to four or more lymph nodes. Unlike these papers, the present study showed no significant change in survival among

Table 3 - Factors that influenced survival rate in five years.

Factor	N° of patients	Five-year Survival (%)	*p*
Lymphadenectomy			0,33
Standard	29	43%	
Radical	21	55%	
Gender			0,8
Male	24	53%	
Female	26	46%	
Lymph node status			0,34
Negative	32	52%	
Positive	18	39%	
Differentiation			0,7
Well/moderately	39	62%	
Poorly	11	31%	
Tumoral invasion			0,2
T1	4	73%	
T2	22	51%	
T3	17	37%	
T4	5	16%	
Transfusion			0,5
Yes	13	58%	
No	37	42%	
Size			0,6
> 2 cm	21	43%	
< 2 cm	29	47%	
UICC			0,42
IA	5	84%	
IB	11	68%	
IIA	17	47%	
IIB	10	36%	
III	7	18%	

groups of patients with positive and negative lymph node status.

Many studies based on lymphatic mapping demonstrated that the pancreatic-duodenal lymph nodes (13 and 17) are the first lymph nodes to be affected by metastatic disease and the other groups are much less frequently envolvidas[19,20,26]. The incidence of lymph node involvement by groups in our population was similar to that described in the literature and the presence of lymph node metastases in other nodal groups without involvement of the pancreato-duodenal group was not observed, suggesting a sequence in the progression of nodal disease. As the incidence of metastasis to lymph nodes out of the pancreato-duodenal group is relatively low, its prognostic significance remains uncertain. In small studies of 35 patients the involvement of the superior mesenteric group was associated with a significantly worse (27%) overall survival at five years when compared with those with positive nodes confined to the pancreatic-duodenal lymph nodes (67%) or patients without nodal involvement[27]. In our series the location of lymph node metastases were not independent prognostic factors, however, Castro et al.[28] demonstrated a significantly lower survival in patients with metastatic para-aortic lymph nodes.

In this work the standard lymphadenectomy (median of 12.3 removed lymph nodes) compared with radical lymphadenectomy (median of 26.5 removed lymph nodes), except for the number of resected lymph nodes, showed no statistically significant difference in the number of patients with positive lymph nodes as well as the change in the pathological staging. Gutierrez et al.[12] suggested that, in GPD, the resection of 10 lymph nodes would be the minimum for adequate staging, which could justify the appropriate staging already achieved by standard lymphadenectomy, where the median number of lymph nodes resected was 12.3.

We conclude from this study that the groups of lymph nodes of the pancreato-duodenal chains (No. 13 or 17) were affected in all patients with positive lymph nodes, suggesting a pattern of lymph node spread.

Despite the radical lymphadenectomy display a longer surgical time when compared to standard lymphadenectomy, there were no statistically significant differences in relation to perioperative blood transfusion, surgical complications, hospital stay, operative mortality, disease-free and overall survival.

The median number of lymph nodes resected was higher in radical lymphadenectomy (26.5) when compared to standard lymphadenectomy (12.3), which did not represent a gain in nodal positivity.

Due to the small number of cases and the limitations of a retrospective study, we suggest that further prospective studies with larger samples be performed to evaluate the real role of lymphadenectomy in adenocarcinoma of the duodenal papilla.

R E S U M O

Objetivo: *avaliar a morbidade e a mortalidade cirúrgica em pacientes submetidos a gastroduodenopancreatectomia (GDP) com linfadenectomia padrão e radical para adenocarcinoma de papila, analisando os fatores prognósticos com relação à sobrevida global e livre de doença.* ***Métodos:*** *foram analisados retrospectivamente no período de 1999 a 2007, no Serviço de Cirurgia Abdômino-Pélvica do INCa-RJ, 50 casos de GDP para adenocarcinoma da papila duodenal divididos em dois grupos de acordo com a linfadenectomia (grupo A: linfadenectomia padrão e grupo B: linfadenectomia radical).* ***Resultados:*** *A mediana de idade foi semelhante nos dois grupos, assim como a distribuição entre os sexos. Na comparação entre as linfadenectomias somente o número de linfonodos ressecados (grupo A: 12,3 e grupo B: 26,5) e o tempo operatório (grupo A: 421 e grupo B: 474) foram significativamente diferentes. Não ocorreram diferenças estatisticamente significativas nos dois grupos com relação a morbi-mortalidade operatória e tempo de internação. A sobrevida livre de doença (grupo A: 35 meses e grupo B: 51 meses) e sobrevida global (grupo A: 38 meses e grupo B: 53 meses) foi maior no grupo da linfadenectomia radical, porém não foram significantes estatisticamente.* ***Conclusão:*** *no presente estudo não ocorreram casos de linfonodos metastáticos para outros grupos nodais sem o acometimento linfonodal das cadeias pancreato-duodenais (13 e 17), sugerindo um padrão de disseminação linfonodal. Apesar da linfadenectomia radical apresentar taxas de sobrevida livre de doença e sobrevida global maiores esses dados não foram significativos estatisticamente. Novos estudos devem ser realizados para avaliar o real papel da linfadenectomia radical no adenocarcinoma da papila duodenal.*

Descritores: *Excisão de linfonodo. Adenocarcinoma. Ampola hepatopancreática.*

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