Annals of Oncology **10** *Suppl. 4*: S281-S284, 1999.
© 1999 *Kluwer Academic Publishers. Printed in the Netherlands.*

Original article

Quality of life, nutritional status and gastrointestinal hormone profile following the Whipple procedure

Robin S. McLeod

Head, Division of General Surgery, Mount Sinai Hospital, Professor of Surgery, University of Toronto, Toronto, Ontario, Canada

Summary

Pancreatic cancer is the second commonest gastrointestinal cancer, after colorectal cancer, in Canada, and most other European and North American countries. Unfortunately, most patients present with advanced locoregional or metastatic disease. For the 10-20% of patients who have localized disease, pancreatic resection is generally the preferred treatment option. Because pancreaticoduodenectomy can be performed safely in expert hands, it has become a more accepted procedure for patients with pancreatic cancer. Furthermore, it has also meant that there is increasing scrutiny of the longterm outcome of patients, especially their nutritional status and quality of life. In a study of 25 unselected patients who had had a Whipple procedure at least 6 months previously and were not known to have residual or recurrent disease, patients appeared to have few gastrointestinal symptoms compared to control patients. However, none of the subjects appeared to be clinically malnourished. Dietary intake and lean body mass were comparable to that of the control group. Quality of life was excellent in these patients. The mean utilities were 0.98 and 1.0 suggesting near normal wellbeing. Similarly, results using the SIP and GIQLI suggested no/minimal impairment in general wellbeing and gastrointestinal function. Two other studies suggest that median survival and performance status are improved in patients having a resection, but it may be due to their disease being more favorable rather than the treatment being beneficial. Further studies objectively assessing the quality of life of all patients undergoing treatment for pancreatic cancer at the various disease stages are required.

Key words: hormone profile, nutrition, quality of life, Whipple

Introduction

Pancreatic cancer is the second commonest gastrointestinal cancer, after colorectal cancer, in Canada, and most other European and North American countries. The incidence is estimated to be approximately 8-9 per 100,000 with 2,900 new cases reported in Canada in 1998 [1]. Unfortunately, most patients present with advanced locoregional or metastatic disease. Thus, the overall 5 year survival rate is dismal at less than 10%. Furthermore, most patients die within the first year following diagnosis.

For the 10-20% of patients who have localized disease, pancreatic resection is generally the preferred treatment option. However, since most tumours are located in the head of the pancreas, this generally means a pancreaticoduodenectomy (Whipple procedure). Although the procedure is usually performed with a curative intent, it may potentially be beneficial as a palliative procedure in prolonging survival and improving quality of life and pain control. However, the Whipple procedure is a technically complex operation which includes the removal of the distal stomach, duodenum, first part of the jejunum, pancreatic head, lower end of the common bile duct and gall bladder so there are also concerns related to the performance of this procedure because of the high associated operative morbidity and mortality rates. This is of particular concern since it is a palliative procedure in most patients.

While operative mortality rates of 20% have been reported in the past, more recently operative mortality rates of 0-5% have been reported [2-5]. In a series of 64 patients who had a palliative pancreaticoduodenectomy, Lillimoe and colleagues from Johns Hopkins University reported the hospital mortality was 1.6% which was similar to that of a group who underwent a palliative bypass procedure [5]. Complications can be significant including bile leaks, fistulas and bleeding. However, again, Lillimoe and colleagues reported similar post-operative morbidity rates (42% versus 32%) for patients undergoing resection or a bypass procedure. Because pancreaticoduodenectomy can be performed safely in expert hands, it has become a more accepted procedure for patients with pancreatic cancer. Furthermore, it has also meant that there is increasing scrutiny of the long term outcome of patients, especially their nutritional status and quality of life.

Nutritional status

Because of the major resection of the gastrointestinal and biliary tracts and pancreas, gastrointestinal dysfunction is a possibility with symptoms of dumping, delayed gastric emptying, early satiety and reflux as well as malabsorption due to pancreatic exocrine and endocrine deficiency. Our group studied 25 unselected patients who had had a Whipple procedure at least 6 months previously and were not known to have residual or recurrent disease [6]. These were compared to a control group of 25 patients who had undergone a cholecystectomy during the same time period. In each group, there were 13 males and 12 females, with a mean age of approximately 58 years. On average, the respective procedure had been performed 5 years previously. Both groups were surveyed with respect to their gastrointestinal symptomatology. As shown in Table I, there were no significant differences between the groups although slightly more patients in the Whipple group appeared to be restricted in the amount of food they could ingest and were

Table 1: Gastrointestinal symptomatology

	Whipple Group				Control Group			
	None	Mild	Mod	Sev	None	Mild	Mod	Sev
Dietary restrictions	17	7	1	0	21	4	0	0
Fullness	19	5	1	0	17	8	0	0
Fullness after eating	20	4	1	0	19	5	0	1
Burping	18	3	4	0	16	7	1	1
Heartburn	13	9	3	0	16	6	2	1
Vomiting*	24	1	0	0	24	0	1	0
Early dumping	24	1	0	0	24	1	0	0
Late dumping	24	1	0	0	24	1	0	0
Greasy Bms	20	2	1	2	25	0	0	0
Jaundice*	25	0	0	0	25	0	0	0
Fever/chills*	23	2	0	0	23	2	0	0
RUQ pain*	21	4	0	0	21	1	3	0
Incisional pain*	22	3	0	0	24	0	1	0

* never/rarely/seldom/always

affected by heartburn and greasy bowel movements. Only 1 patient in each group complained of mild early or late dumping. Patients with a pylorus sparing pancreatico-duodenectomy appeared to be less likely to complain of burping and fullness after eating (1of 9 versus 4 of 16), be restricted in the volume of food intake (1 of 9 versus 7 of 16) but were more likely to complain of heartburn (6 of 9 versus 4 of 16) although none of these differences were statistically significant. Similarly, Patti and colleagues reported that 8 of 10 patients who had a pylorus sparing procedure were free of gastrointestinal symptoms [7].

The post-operative nutritional status of subjects is listed in Tables II and III. Six patients follow a diabetic diet plus 1 required insulin and 3 required oral hypoglycemic agents. One patient in the Whipple group took pancreatic enzyme supplements (cotazyme) and also complained of difficulty maintaining his weight.

There were no significant differences in their nutritional parameters. Formal studies to assess absorption were not performed. However, none of the subjects appeared to be clinically malnourished as judged by the Subjective Global Assessment. Dietary intake was comparable to that of the control group. The mean postoperative weight of the Whipple patients was greater than their mean preoperative weight and was also greater than their ideal weight. There was no significant difference in lean body mass or in dietary intake between the two groups. Skeletal and respiratory muscle function studies, which assess physical performance, also failed to reveal any significant differences between the groups nor between patients having a standard or pylorus sparing procedure [8].

The gut hormone status of patients was also assessed in this study. There were no significant differences in the mean basal, peak or integrated postprandial responses of the gut hormones with the exception of pancreatic polypeptide and gastrin (in patients having a standard Whipple procedure). The absence of postprandial pancreatic polypeptide responses in both Whipple groups is consistent since the head of the pancreas is the major source for pancreatic polypeptide [9]. Although diabetes may constitute a significant problem after a conventional Whipple procedure, the results of this study suggested that postprandial insulin responses were well maintained after both Whipple procedures.

Table 2: Post operative status

	Whipple Group	Control Group
Current Medications		
Insulin	1	0
Oral hypoglycemics	3	0
Cotazyme	1	0
H_2 Blocker	3	3
Prokinetic Agent	0	0
Dietary Restrictions		
Diabetic Diet	6	0
Low fat	4	6
Low Calorie	1	3
High fiber	0	1
Dietary restrictions-avoid certain foods	18	12
Milk Intolerance	5	6
Restricted Amount of Food	4	4
Mean # meals	4.2	4.0
Mean # Bms/day (post-op)	1.6 ± 0.9	1.4 ± 0.8
Mean # Bms/day (pre-op)	1.3 ± 0.7	1.2 ± 0.5
Difficulty maintaining weight	1	0

Quality of life assessment

There is increasing recognition that quality of life is an important outcome in clinical medicine, especially in conditions such as pancreatic cancer where the disease is fatal in most patients. Despite this, there is still little consensus on what is meant by quality of life. Generally, experts agree that quality of life includes the domains of physical, emotional and social well-being. Somatic sensation (ie: pain) and functional ability may also be important components [10]. The World Health Organization definition of health as being "a state of complete physical, mental and social well-being and not merely the absence of disease" has been adopted by many [11]. In the area of pancreatic cancer, there has been little attention paid to quality of life until recently. Fitzsimmons and Johnson reported that between 1980 and 1992, there were only 15 articles where quality of life was discussed [12]. However, there is also evidence of increasing interest in this area in that there were 25 articles published during the 1 year period of 1996 which mentioned quality of life.

In the same study that was mentioned previously, our group compared the quality of life of patients who had had a Whipple procedure to those who had had a cholecystectomy [6]. This study did not attempt to answer the broader question of quality of life of patients suffering from pancreatic cancer which of course is important. It only addressed the issue of the effect of a Whipple procedure on quality of life.

Quality of life was measured using several techniques and instruments. The time tradeoff technique (TTO) and the direct questioning of objectives (DQO) are methods for ascertaining utilities [13-17]. Utilities may range from 0 signifying death to 1 signifying normal health. Both of these instruments have been used previously to ascertain utilities in different health states. In addition, 2 psychometric instruments were used. The Sickness Impact Profile (SIP) is a generic instrument used to measure general health status [18]. Scores range from 0 to 100.3 with higher scores indicating poorer health. A second disease specific instrument, the Gastrointestinal Quality of Life Index (GIQLI) was also used [19]. It is a self-administered index which consists of 32 items pertaining to gastrointestinal function with scores ranging from 0 to 4 so the highest possible score is 132. A high score indicates no impairment of quality of life. It has been used previously to assess quality of life following laparoscopic cholecystectomy. The results of the quality of life assessments are shown in Table IV. The mean utilities of the Whipple patients, using both instruments, were 0.98 and 1.0 suggesting near normal wellbeing. Similarly, results using the other instruments suggested no/minimal impairment in general wellbeing and gastrointestinal function. There were no significant differences between the Whipple patients and the control subjects. Because of the uniformly good results, analysis of factors affecting quality of life was not performed.

Kokoska and colleagues extracted data on outcome in patients with pancreatic cancer from a US Department of Defense database which collected information from over 100 institutions [20]. Between 1989 and 1996, there were 822 patients treated for pancreatic cancer. There were 168 who underwent a resection (124 had a Whipple procedure), and these were compared to those who were not resected. The resection group lived longer (mean 16.3 months versus 6.1 months). As well, quality of life was assessed using the Karnofsky Performance Score and found to be significantly improved in patients with Stages I-II cancers who underwent a resection (mean KPS 79 versus 65 for the unresected group). Those with Stage III cancers did not have improved scores. The Karnofsky Performance Score mainly assesses functional status or physical well-being and therefore is unidimensional and does not measure quality of life in the broader sense. The results obtained in this study probably reflect the fact that patients with Stage III cancers are more likely to develop a recurrence. Thus, their performance status may not be improved by a resection. Another limitation of this study is that data were analyzed retrospectively and the KPS scores were available only at 1 time point in the patient's history.

Table 3: Nutritional assessment

	Whipple Group	Control Group
Mean Height (cm)	166.9 ± 8.1	171.6 ± 9.6
Mean Weight (kg)	72.5 ± 13.7*	83.9 ± 16.2
Body Mass Index (kg/m2)	26.1 ± 4.9	28.2 ± 4.4
% pre-illness Weight	101.5 ± 20.1	102.3 ± 5.9
% IBW	113.3 ± 4.3	122.3 ± 18.1
Body fat (kg)	18.7 ± 8.9	24.6 ± 8.8
(%wt)	25.5 8.8	28.7 7.4
Lean body mass (kg)	53.5 ± 10.3	59.4 ± 12.3
(% wt)	74.5 ± 8.8	70.9 ± 7.4
Lean:fat ratio	3.6:1	2.6:1
MAC (cm)	29.7 ± 6.8	33.1 ± 3.2
Total Skinfold (cm)	65.0 ± 31.0	83.1 ± 33.8
MAMC (cm)	25.9 ± 3.6	26.1 ± 3.5
Dietary Intake		
kcal/kg.	28.5 ± 1.6	25.6 ± 1.5
Fat (% energy)	32.8 ± 1.5	32.8 ± 1.5
Carbohydrate(% energy)	50.8 ± 2.0	49.8 ± 1.8
Protein (% energy)	16.5 ± 0.8	17.4 ± 0.9

* $p < 0.05$

Bakkevold and colleagues studied 84 patients who had radical surgery for pancreatic cancer and compared them to those who had bypass procedures, laparotomy alone or no surgery [21]. At 3 months post discharge, radically resected patients had the best palliation and clinical performance. Eighty-two percent were mobile and 62% were pain free. The median Karnofsky Performance Score was 80 compared to 70 in the bypass group.

Thus, there are limited data available on the quality of life of patients with pancreatic cancer. It seems that patients who have had a Whipple procedure and do not have recurrence of their disease have an excellent outcome. There are little data on all patients (including those who do develop recurrence). However, it seems that overall patients have an improved quality of life following resection, but it may be due to their disease being more favorable rather than the treatment being beneficial.

Table 4: Quality of life assessments

Whipple Group	Control Group
1.0 ± 0	0.99 ± 0.04
0.99 ± 0.02	0.98 ± 0.05
117.8 ± 6.8	117.4 ± 12.2
1.5 ± 2.3	2.9 ± 4.0

Future work

It is only recently that objective assessment of the various treatments for pancreatic cancer has been performed. More trials are required to compare the various palliative treatment modalities. In so doing, it will be important to include assessment of quality of life. To date, generic instruments have been used to assess quality of life. However, they may lack sensitivity and disease specific instruments may be better. In keeping with the EORTC philosophy of developing a core module for use in all cancer patients and a disease specific module for use in patients with specific cancers, the EORTC has developed the QLQ-PAN26 to be used in conjunction with the core cancer module (QLQ-C30) [12]. This 26 item questionnaire contains 17 items sampling the symptom and side effects domain as well as 9 items sampling the emotional and social consequences of having pancreatic cancer. It has been developed by an international group and is available in 12 languages. Current studies are addressing the validity and responsiveness of this instrument. A well validated instrument such as this should be useful in clinical trials as well as assessment of patients in various stages of their disease.

Conclusions

In summary, there are limited data regarding the quality of life and nutritional status of patients who have had a pancreaticoduodenectomy for pancreatic cancer. Those who remain free of disease following a Whipple procedure appear to have an excellent outcome. These patients suffer from minimal gastrointestinal symptoms and are able to maintain their weight and achieve a high quality of life. Further studies objectively assessing the quality of life of all patients undergoing treatment for pancreatic cancer at the various disease stages are required.

References

1. Canadian Cancer Statistics, 1998.
2. Nakase A: Treatment of cancer of the pancreas and periampullary region: Cumulative results in 57 institutions in Japan. Ann Surg 1977; 185:52
3. Child CG, Hinerman DL: Pancreaticoduodenectomy. Surg Gynecol Obstet 1978; 147:529.
4. Jones BA, Langer B, Taylor BR et al: Periampullary tumors: Which ones should be resected? Amer J Surg 1985; 149:46-52.
5. Lillemoe KD, Cameron JL, Yeo CJ et al: Pancreaticoduodenectomy: Does it have a role in the palliation of pancreatic cancer? Ann Surg 1996;223:718-25.
6. McLeod RS, Taylor BR, O'Connor BI et al: Quality of life, nutritional status, and gastrointestinal hormone profile following the whipple procedure. Am J Surg 1995; 169:179-85.
7. Patti MG, Pellegrini CA, Way LW: Gastric emptying and small bowel transit of solid food after pylorus-preserving pancreaticoduodenectomy. Arch Surg 1987; 122:528-32.
8. Royall D, Jeejeebhoy KN, O'Connor B et al: Nutritional status and function in patients following whipple procedure compared with controls J Amer Coll Nutr 1996; 15:73-8.
9. Greenberg GR, McClay RF, Adrian TE et al. Inhibition of pancreas and gallbladder by pancreatic polypeptide. Lancet 1978;2:1280-2.
10. Schipper H, Clinch JJ, Olweny CLM. Quality of life studies: definitions and conceptual issues. In Quality of Life and Pharmacoecomonics in Clinical Trials (2nd ed.), B. Spilker, editor. Philadelphia, Lippincott-Raven, 1996.
11. World Health Organization: The First 10 Years of the World Health Organization. Geneva, WHO, 1958.
12. Fitzsimmons D, Johnson CD: Quality of life after treatment of pancreatic cancer. Langenbeck's Arch Surg 1998;338:145-51.
13. Torrance GW, Thomas WH, Sackett DL: A utility maximization model for evaluation of health care programs. Health Serv Res 1972; 7:118-33.
14. Mohide EA, Torrance GW, Streiner DL et al: Measuring well-being of family caregivers using the time trade-off technique. J Clin Epidemiol 1988; 41:475-82.
15. Churchill DN, Torrance GW, Taylor DW et al: Measurement of quality of life in end-stage renal disease: The time trade-off approach. Clin Invest Med 1987;10:14-20.
16. McLeod RS, Churchill DN, Lock AM et al: Quality of Life of patients with ulcerative colitis preoperatively and postoperatively. Gastroenterology 1991; 101:1307-13.
17. Detsky AS, McLaughlin JR, Abrams HB et al: Quality of life of patients on long-term total parenteral nutrition at home. J Gen Intern Med 1986; 1:26-33.
18. Berger M, Bobbit RA, Carter WB et al: The sickness impact profile: Development and final revision of a health status measure. Med Care 1981; 19:787-805.
19. Eyspach E, Williams JI, Wood-Dauphine S et al: The Gastrointestinal Quality of Life Index (GIQLI) Development and Validation of a new instrument. Br J Surg 1995;82:216-22.
20. Kokoska ER, Stapleton DR, Virgo KS et al: Quality of life measurements do not support palliative pancreatic cancer treatments. Int J Onco1998;13:1323-9.
21. Bakkevold KE, Kambestad B: Palliation of pancreatic cancer. A prospective multicentre study. Eur J Surg Onco 1995;21:176-82.

Correspondence to:
Dr. R.S. McLeod
Mount Sinai Hospital
600 University Avenue, Suite 449
Toronto, Ontario M5G 1X5
Canada
email: rmcleod@mtsinai.on.ca