

THE OUTCOME OF WHIPPLE PROCEDURE IN THE MANAGEMENT OF EARLY CANCER

Hamza Shirah, MD; Tarek Amin, MD, FRCS

The Whipple procedure has undergone tremendous improvements in the past few years with decreased operative mortality and morbidity rates compared to its early evolution era some 50 years ago.¹⁻⁶ Recent published data report mortality rates of 5% or less⁶⁻⁹ and morbidity rates as low as 25%.¹⁰⁻¹¹ Furthermore, other reports show an improved quality of life of cancer patients with decreased hospital stay and resultant decreased costs.¹² In this article we report our 15 years' experience with the modified Whipple procedure in early-stage cancer patients in a specialized tertiary care center in Saudi Arabia, and compare the results with other published data on patients who have undergone the same procedure.

Patients and Methods

The medical records of 74 patients diagnosed with cancer who underwent Whipple procedure for curative intent between 1985 and 2000 were carefully analyzed. All patients were operated on by the same surgeon (the second author). Pre-operative assessment was uniform with all patients (CBC, renal and hepatic function tests, coagulation profile, and amylase level, CT scan of the abdomen, pelvis and chest, endoscopic retrograde cholangio-pancreatography, bone scan, chest x-ray, and electrocardiogram). Nutrition was assessed by albumen level, hydration, and electrolyte balance. Postoperative management and intensive care support were similar in all patients. Patients were followed for 5 years post-operatively with repeat CT scan of the abdomen every 6 months to detect recurrence, and blood work for nutrition and amylase level. Inclusion criteria included: Early stage cancer [localized lesion, no local or distant metastasis, no lymph nodes involvement], early detection [short period of symptoms], average to good body build [weight loss not

exceeding 10 kg. in 3 months], and no major disabling comorbid disease. We excluded cases done for palliative intent, benign diseases and trauma.

All patients had the same operative technique. We used the rooftop upper abdominal incision for better exposure of the field. Our modified resection comprised a 20% partial gastrectomy [non pylorus preserving], meticulous duodenectomy to avoid bleeding from the small numerous venous tributaries to the portal vein [often fatal if haemorrhage encountered], common bile duct resection high close to the confluence [to provide a wider anastomosis and minimize stenoses], cholecystectomy, and the head of the pancreas was resected to the left of the portal vein [as the last resected organ to minimize intra-abdominal exposure to pancreatic secretions]. Reconstruction was done as end-to-side pancreaticojejunostomy in two layers [outer 2-0 silk, and inner 3-0 maxon] with insertion of a 12 centimetres small (5 millimetres) feeding tube into the main pancreatic duct [5 centimetres in that end, and 7 centimetres into the jejunal end] to prevent leakage of pancreatic contents and breakage of anastomosis, wide [6 centimetres] end-to-side hepaticojejunostomy also in two layers, and gastrojejunostomy (stapled vertically at 2 centimetres from the resection side). All patients had nasogastric tube (removed when drainage was less than 300 ml/day) and 2 Jackson Pratt drains draining the hepaticojejunostomy site and pancreaticojejunostomy site, which were removed when drainage was less than 30 ml/day, after sampling for amylase levels (in the collected fluid) to check for pancreatic leak. Patients were started on oral feeding between 4th and 5th post-operative day. Complications were classified into minor general (non-procedure related) or major surgical when the procedure technique was the main contributing factor. Operative mortality was defined as death in the hospital during or after the procedure before discharge. Patient quality of life was measured during outpatient clinic visits in regard to being symptom free, no recurrence, and the ability to conduct normal life activities, weight gain, and nutritional markers.

From the Department of Surgery, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia

Address reprint requests and correspondence to Dr. Shirah:
Department of Surgery, MBC-40 King Faisal Specialist Hospital & Research Centre, P.O. Box, 3354, Riyadh 11211, Kingdom of Saudi Arabia.

Accepted for publication

Results

48 patients (64.9%) were male and 26 (35.1%) were female. The average age was 63 and 51 years respectively. The patient's population data showed variable distribution from all regions of the Saudi Arabia (see table 6). Co morbid disease was present in 47 (73.5%) patients with 27 patients having 2 or more of these factors. 14 (18.9%) patients had diabetes mellitus, 8 (10.8%) had hypertension and 4 (5.4%) had ischemic heart disease, while 39 (52.7%) presented with malnutrition (evident by low, deranged nutritional marker [albumen]) (see Table 1). The majority of patients - 56 (75.7%) presented with abdominal pain. 47 (73.5%) had history of weight loss, 43 (58.1%) had loss of appetite, 34 (45.9%) had obstructive jaundice, 18 (24.3%) had vomiting. In 3 (4%) cancer was an incidental finding (2 post cholecystectomy and 1 post endoscopy) (see Table 2). The duration of symptoms ranged between 9-15 weeks in males and 6-14 weeks in females.

The histopathological diagnosis showed a predominance of ampullary cancer (44.4%), followed by cancer of the head of the pancreas, cholangiocarcinoma and cancer of the duodenum respectively (see table 3). All patients had free resection margins. The average operative time was 6.5 hours (surgery and anesthesia) with an average actual surgical time of 5 hours. The estimated average of blood loss was 600 ml, 24 (32.4%) patients required 1-2 units of whole blood transfusion (16 [66.7%] male and 8 [33.3%] female).

Average total hospital stay was 18.5 days, for which an average of 5.5 days were used for pre-operative preparation and nutritional build up, 13 (17.6%) required preoperative total parenteral nutrition [TPN] for 1 week and 17 (23%) patients needed post-operative TPN. The average intensive care unit stay post-operatively was 3.5 days. The overall morbidity rate was 38.1% (see Table 4). Minor complications accounted for 31.7% and major surgical complications for 4.8%. 2 (3.2%) patients had central venous catheter infection, 7 (11.11%) atelectasis, 1 (1.6%) pleural effusion, 4 (6.34%) had wound infection in which 2 patients needed removal of staples for irrigation. 2 patients required bedside wound debridement, 1 patient had intra-abdominal bleeding post-operatively (drained 400ml of blood in the first 4 hours in the intensive care unit), which was managed conservatively with blood transfusion (hemoglobin was 8.5). Correction of coagulation factors by transfusion of fresh frozen plasma (PT 19.5 and PTT 37.8) and bleeding settled within 6 hours (total drainage of 950ml). 4 (6.34%) patients had lymphatic leak (evident by high output drainage of chyle) treated conservatively by restricting oral intake and total parenteral nutrition until the drainage settled down to minimal or nil. 1 (1.6%) patient had sepsis while in intensive care unit (3rd post-operative day) with positive blood cultures of *Staph. aureus* managed by intra-venous vancomycin for 1 week with subsequent resolution of sepsis, 1 (1.6%) patient had pulmonary embolism on the third post-operative day (complained of dyspnea, with oxygen saturation of 84%)

diagnosed by spiral CT scan and managed by intra-venous heparin infusion and warfarin subsequently.

The major surgical complications consisted of 2 (3.2%) patients who developed hepaticojejunostomy stenosis. 1 patient presented with cholangitis, which required admission, intravenous antibiotic coverage and urgent percutaneous transhepatic cholangiogram (PTC), and dilatation. He responded well to the procedure and follow-up PTC showed no recurrence. The other patient presented 3 months post operatively with jaundice and right upper quadrant pain. She required several re-admissions for PTC and dilatation. 1 (1.6%) patient had gastrojejunostomy outlet obstruction due to adhesions (presented 5 weeks post-operatively with recurrent vomiting and diagnosed by gastrograffin). He required re-admission and re-operation for release of the adhesions and reconstruction gastrojejunostomy. No other post gastrectomy complications were reported. There was no anastomotic leak, no biliary fistula, no pancreatic fistula, and the operative mortality rate was zero 0. The 5 year (period of follow-up) survival rate was 77% (80.5% in male patients compared to 72.7% in female patients). Recurrence rate (within 5 years follow-up) was 19% (see Table 5); 4 (6.3%) patients died within 1 year [1 of them died 7 months after surgery due to massive myocardial attack and the remaining 3 died 9, 11 and 12 months post-operatively respectively due to cardio-pulmonary arrest], and 10 (15.9%) patients died during the following 3 years.

All the patients reported a better life quality during their post operative course, 74 (100%) were free of symptoms, 39 (52.7%) gained less than 5 kilograms, 13 (17.6%) gained less than 10 kilograms, and 11 (14.9%) gained less than 15 kilograms, 53 (71.6%) were able to perform full normal daily activities, and the rest 21 (28.4%) were able to perform partial daily life activities (mostly due to old age, not related to surgery). Albumen and electrolytes were normal in all patients.

Discussion

The Whipple procedure, which is used for treatment of malignant and benign diseases either for curative or palliative intent¹⁰⁻¹³, has passed through several stages of improvement in regard to mortality and morbidity rates. Although early published data reported disappointing high mortality rates¹⁶⁻¹⁷, recent published data showed a mortality rate as low as 0-9%¹⁻⁹ and morbidity rates of 25% or less^{8, 18}. A recently published article reviewed published data since 1990 with more than 100 cases¹⁴, which showed an example of the latest improvement in mortality outcome, 3 articles reported 0 mortality, and 5 reported less than 5%, while the majority reported morbidity rates between 17.8 and 52%.

Although the Whipple procedure remains an effective treatment for many intra-abdominal malignancies with curative intent, it is still considered a very risky and

Formatted

hazardous procedure dealing with vital anatomical structures. The procedure affect several physiological functions of the human body which exert major influence on the patient's life quality and subjects the surgeons to tremendous stress and a very tough challenge¹⁵. Not only because of the high mortality rates but also due to its association with some serious complications like developing a biliary fistula, pancreatic fistula and delayed gastric emptying²¹⁻²⁴, for which many surgeons modified the procedure trying to overcome such complications. Some of the published reports showed encouraging data³⁴ while other articles reported no significant change in the outcome between the modified procedures and the standard one²⁵⁻²⁶. Many patients who survive the procedure suffer from significant gastrointestinal symptom, pancreatic exocrine and endocrine deficiency affecting their life quality and subjecting them to additional agony and disability²⁷⁻³⁰.

The quality of life in patients who survived the procedure and remained disease free was a subject for debate among surgeons for the justification of Whipple procedure. Two articles thoroughly looked at this and reported encouraging results of quality of life after Whipple procedure for benign and malignant diseases³¹⁻³². In our report, the majority of patients had an excellent quality of life with minimal or no influence on their body functions measured during out patient follow up by the ability to carry out daily activities, remain free of symptoms, and gain weight in addition to social and psychological adjustment, except for one patient who developed hepaticojejunostomy stenosis which required multiple PTC and dilatation. We report only early stage cancer patients operated on for curative intend and excluded all cases operated for palliative reasons for advanced disease, benign diseases, and trauma.

Our results of low morbidity and no operative mortality with good quality of life resembles other results reported all over the world, and should encourage other to follow a similar approach. These results should be attributed to the early detection of the disease, quick referral, well planned approach in the form of proper work up, careful patient selection, meticulous conduction of the procedure, in addition to the other factors including the surgeon, the hospital facilities, and other supporting services.

References

1. Calver J. Occupational Health Services. American J infection control 1997; 25(5): 363-5.
2. Al Faleh F Z, Facharzt. Hepatitis B infection in Saudi Arabia. Ann Saudi Med 1988; 8: 474-9.
3. Fathalla SE, Namnyak SS, Al Jama A, Rabaria Bautista MM. The prevalence of hepatitis B surface antigen in healthy subjects residents in the Eastern province of Saudi Arabia. Saudi Med J1985; 6:236-9.
4. Fathalla SE, Al Jama AA, Badawy MS, et al. Prevalence of Hepatitis C infection in the Eastern Province Saudi Arabia by RE-DNA second generation and supplemental EIA tests. Saudi Med J1994; 15:11-3.

5. Al Faleh F Z, Ramia S. Hepatitis C virus (HCV) infection in Saudi Arabia: a review. Ann Saudi Med 1997; 17:77-82.
6. Bahakim H, Bakir TMF, Arif M, Ramia S. Hepatitis C virus antibodies in high risk Saudi groups. Vox Sang 1991; 60:162-4.
7. Bernvil SS, Sheth K, Ellis M, et al. HIV antibody screening in Saudi Arabian blood donor population: five years experience. Vox Sang 1991; 61:71-3.
8. Gerberding JL. Management of occupation exposures to blood borne viruses. N Engl J Med 1995;332: 444-51.
9. Manian FA. Hepatitis C after needle stick injuries. Ann Intern Med 1992; 116:345-6.
10. Puro V, Petrosilla N, Ippolito G. Italian Study Group On Occupation Risk Of HIV and Other Blood borne Infections. Risks of hepatitis C seroconversion after occupational exposure in health care workers. Am J Infect Control 1995; 23: 273-7.
11. Gerberding JL. Incidence and prevalence of human immunodeficiency virus, hepatitis B virus, hepatitis C virus and cytomegalo virus among health car personnel at a risk of blood exposure: a final report from a longitudinal study. J Infect Dis 1994;170:1410-1417.
12. Hanrahan A, Reutter L. A critical review of literature on sharps injuries: epidemiology, management of exposures and prevention. J Adv Nurs 1997; 25:144-154.
13. EPINet. Exposure prevention information network data reports. University of Virginia: International Health Care Worker Safety Center.
14. Mujeeb A S, Khatri Y, Khanani R. Frequency of parenteral exposure and seroprevalence of HBV, HCV and HIV among operation room personnel. J Hosp Infect 1998; 38:133-7.
15. Roy E, Robillard P. Underreporting of accidental exposures to blood and other body fluids in health care setting: an alarming situation. Adv Exposure Prev 1995; 1(4): 11-13
16. Poole CJM, Miller S, Fillingham G. Immunity to hepatitis B among health care workers performing exposure prone procedures. BMJ 1994; 309: 94-95
17. Barone P, Sciacca A, Lupo F, Leonardi S, Murumeci S. Hepatitis B vaccination in young nurses of a general hospital. Ann Ig 1995; 7(4): 251-255.
18. CDC (Centers of Disease Control and Prevention). Recommendations for post exposure prophylaxis (PEP) foe Exposure to HBV, HCV and HIV. MMWR 2001; 50:22.
19. Ruben FL, Norden CW, Rockwell K, Hruska. Epidemiology of accidental needle puncture wounds in hospital workers. Am J Ed SCI 1983; 286(1): 26-30.
20. 29 CFR 1910.1030; Occupational safety and Health Administration: final rule on occupational exposure to blood borne pathogens. 56 Fed Reg. 64004 (1991).
21. CDC (Centers of Disease Control). Perspective in disease prevention and health promotion update. Universal precautions for prevention of transmission of HIV, HBV and other blood borne pathogens in health care settings. MMWR1988; 37:24.
22. Yassi A, McGill ML, Khokhar JB. Efficacy and cost effectiveness of a needleless intravenous access system. Am J infect Control 1995; 23 (2): 57-64.

Deleted: