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Evolution of the Whipple procedure at the Massachusetts General Hospital

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Abstract

Background—Since Allen O. Whipple published his seminal paper in 1935, the procedure that bears his name has been performed widely throughout the world and is now a common operation in major medical centers. The goal of this study was to investigate the evolution of pancreatoduodenectomy at the Massachusetts General Hospital (MGH).

Methods—We sought to identify all pancreatoduodenectomies performed at the MGH since 1935. Cases were obtained from a computerized database, hospital medical records, and the MGH historical archive. Demographics, diagnosis, intraoperative variables and short-term surgical outcomes were recorded.

Results—The first pancreatoduodenectomy at the MGH was carried out in 1941; since then, 2,050 Whipple procedures have been performed. Pancreatic ductal adenocarcinoma was the most frequent indication (36%). Pylorus preservation has been the most important variation in technique, accounting for 45% of Whipple procedures in the 1980s; observation of frequent delayed gastric emptying after this procedure led to decline in its use. Pancreatic fistula was the most frequent complication (13%). Operative blood replacement and reoperation rates have decreased markedly over time; the most frequent indication for reoperation was intra-abdominal bleeding. Mortality has decreased from 45% to 0.8%, with sepsis and hypovolemic shock being the most frequent causes of death. Mean duration of hospital stay has decreased from >30 to 9.5 days, along with an increasing readmission rate (currently 19%).

Conclusion—The Whipple procedure in the 21st century is a well-established operation. Improvements in operative technique and perioperative care have contributed in making it a safe operation that continues evolving.

Allen Oldfather Whipple is the uncontested father of North American pancreatic surgery. Although both Alessandro Codivilla in Italy and Walter Kausch in Germany had performed pancreatoduodenectomy decades before,^{1–3} Whipple's presentation at the American Surgical Association meeting in 1935 of 3 patients who underwent a 2-staged operation⁴ and his successful performance of a 1-stage pancreatoduodenectomy 5 years later⁵ set the stage for further development of this operation in the United States and Canada. The current version of the operation that bears his name is now performed throughout the world and, although still fraught with potential serious complications, is a common operation in many major medical centers. The goal of this study was to investigate the evolution of pancreatoduodenectomy at the Massachusetts General Hospital (MGH), including its

indications, technique, outcomes, and lessons learned during the 75 years that have elapsed since Whipple's initial report.

PATIENTS, METHODS, AND SOURCES

We sought to identify all pancreatoduodenectomies performed at the MGH since 1935. Cases performed from 1990 and up to August 2011 were identified from a computerized, institutional review board-approved database on pancreatic resections kept in the Department of Surgery and updated on a regular basis. This database contains both clinical and pathologic information. Cases from 1961 to 1989 were identified from a manual filing system based on common operative procedure codes that was created and kept in the MGH department of Medical Records and Health Information Systems. From those medical record numbers, the original charts were retrieved and reviewed. Cases labeled "Whipple procedure," "pancreatoduodenectomy," or "resection of the head of the pancreas" from before 1961 were identified from the log books of the operating room or anesthesia. The logbooks up to 1946 were obtained from medical records and those before that from the MGH historical archive. With the help of its curator, Mr. Jeffrey Mifflin, we attempted to find the first pancreatoduodenectomy performed at the MGH. Unfortunately, operating room and anesthesia logbooks from the 1930s and 1940s had been kept in the basements of buildings that suffered from regular flooding, with some of the books being lost as a consequence. We found the books from 1940 to 1946, but books corresponding to the earlier years (which were at the bottom of the pile) were lost in the floods.

Demographics, diagnosis, operative technique, duration of the operation, estimated blood loss (EBL), blood replacement, operative complications, reoperation, postoperative death, duration of stay, and readmissions for operative complications were recorded for each patient as available.

RESULTS

Our search identified 2,050 Whipple procedures performed between 1940 and 2011 (Fig 1). The earliest pancreatoduodenectomy that we could find was performed by Dr Claude E. Welch in 1941 for an "adenoma of the head of the pancreas." The moniker "Whipple procedure" was first utilized in 1947, 12 years after Whipple's publication.

The surgeons

In the 1940s, 11 pancreatoduodenectomies were performed at the MGH by 7 different surgeons: Arthur W. Allen, Claude E. Welch, Marshall K. Bartlett, Leland S. MacKittrick, Howard Ulfelder, and Gordon Donaldson. For a time, the procedure remained infrequent, with 26 surgeons performing only 52 cases between 1941 and 1969 (~2 per year). Of those, 20% were performed by Dr Welch. In the 1970s, the number of Whipple procedures tripled, with 18 surgeons performing 61 operations (~6 per year). In that decade, Dr George L. Nardi performed 25% of the procedures. There was again a tripling in the decade of the 1980s, with 209 Whipple resections performed (~21 per year), and this number then increased by 130% to 476 patients in the 1990s (~48 per year). The 1980s and 1990s were characterized not only by a marked increase in the number of operations, but also the rise of pancreatic surgery as a specialty. During this period, Dr Andrew L. Warshaw performed 64% of the 685 operations, and 29 other surgeons operated on the rest of the cases. The first decade of the 21st century has seen marked further expansion in the numbers: 1,252 Whipple operations were performed from 2000 until August of 2011 (~125 per year), a 2.6-fold increase from the previous decade. Two surgeons (ALW and CFC) operated on 77% of the cases, and a group of 5 surgeons accounted for 86% of the operations. The remaining 14% were operated on by 18 different surgeons.

The patients

There were 1,041 (51%) males and 1,009 (49%) females with a mean age of 62 years (standard deviation, 13.7). The youngest patient in our series was a 3-day-old newborn who underwent a Whipple for nesidioblastosis in 1989. Remarkably, the child tolerated the procedure very well and was discharged home on postoperative day 19. The oldest patient, a 92-year-old woman with an ampullary carcinoma, recovered uneventfully.

Indications—Pancreatic ductal adenocarcinoma (PDAC) was the most frequent indication for performing a Whipple procedure, accounting for 35% of cases (Fig 2). Cystic neoplasms and ampullary lesions were the second and third most common indications (17% and 16%, respectively). The indications for operation have changed over time. In the 1940s, PDAC was the indication for 9 of the 11 Whipple procedures; the remaining 2 cases were a duodenal cancer and a cholangiocarcinoma. Between 1950 and 1969, 49% of Whipples were performed for pancreatic cancer, and ampullary lesions emerged as an indication (12%). Duodenal cancer and chronic pancreatitis accounted for 7% each, with small numbers of other diagnoses completing the list. Between 1970 and 1989, the proportion of PDAC (32%) continued to decline as other indications increased. Chronic pancreatitis reached its peak in this period and was the indication for 20% of resections, followed by ampullary lesions (18%). In that era, a modest 6% were operated for a pancreatic cystic neoplasm. Over the last 2 decades, the proportion of PDAC remained stable (35%), but cystic neoplasms emerged as the second most frequent indication for a Whipple procedure, now accounting for 18%. Ampullary lesions and chronic pancreatitis were the indication for operation in 14% and 11% of the cases, respectively.

The operation

Operative technique—In our first 10 years, 3 of the 11 Whipple resections were performed in 2 stages as described originally by Dr Allan Whipple in his seminal paper. In these 3 cases, the first stage involved (1) choledochojejunostomy plus enteroenterostomy, (2) cholecystostomy plus jejunostomy, and (3) choledochostomy plus cholecystoduodenostomy, respectively. The second-stage procedure involved the pancreatoduodenectomy plus pancreatojejunostomy (the prior biliary-enteric drainage was left as is). The times between the first and second stages were 27, 12, and 33 days. Prophylactic femoral vein ligation, common at that time, was performed shortly after the first stage in 3 cases. Since August, 1947, all Whipples at MGH have been performed in a single stage (and prophylactic venous ligation went out of practice). Figure 3 shows a diagram drawn by a surgical resident depicting the reconstruction after a Whipple procedure in 1947. Notice that the jejunal limb was brought in the bed of the duodenum through the gap left at the ligament of Treitz, that the gallbladder was left in situ, and that the bilioenteric anastomosis was done in an end-to-end fashion.

Technique variations—For a time, preservation of the pylorus (ie, no antrectomy) was the single most frequent variation of the Whipple operative technique. Dr Warshaw in 1981 was the first MGH surgeon to use this technique. Pylorus-preserving Whipple resections reached a peak between 1985 and 1990 when 45% of all resections were done in this manner. Observation of frequent delayed gastric emptying after this procedure⁶ and a subsequent decrease in the incidence of this complication by reverting to a distal gastric resection with no adverse nutritional effect⁷ led to gradual decline in the use of pylorus preservation, now accounting for <1% of the procedures performed in the last 6 years (Fig 4).

Vascular resection/repair—Venous vascular resections were performed in 71 cases (3%). These were very infrequent in the 1980s, but in the last decade 4% of all

pancreatoduodenectomies included resection of the portal and/or superior mesenteric vein. Indeed, 11% of the pancreatoduodenectomies for pancreatic cancer included a vein resection.

Intraoperative blood loss and blood replacement—There was no consistent or detailed information in patients' medical records between 1940 and 1964 regarding intraoperative EBL. Subsequent data show that operative EBL decreased over time. The mean EBL of 1,760 mL in the 1960s has declined to 764 mL in the last 2 decades. From 1940 through 1969, every patient who underwent a Whipple procedure was transfused. Between 1970 and 1984, the frequency of transfusion was still 85%. Since 1985, the proportion of patients being transfused has decreased steadily to an average of 13% over the last 10 years (Fig 5, A).

Operative time—Operative time was the least in the 1940s, when Whipples were performed in a mean of 277 minutes, perhaps reflecting the perceived need for speed at a time when the duration of the anesthesia corresponded with the risk of postoperative pneumonia and perhaps to less meticulous technique. The peak operative time was reached between 1975 and 1980, when the mean duration of a Whipple was 438 minutes. In the most recent 5 years, the mean operative time has been 347 minutes (Fig 5, B).

Clinical course

Postoperative death—There have been 50 deaths related to operative complications, accounting for 2% of all Whipple resections at the MGH. The 2 most frequent causes of death were sepsis and hypovolemic shock secondary to intra-abdominal bleeding (24% each; Table I). No patient in this series died intraoperatively. There has been a steady decline in the operative mortality over time (Fig 5, C). In the 1940s, 45% of the patients who underwent a Whipple procedure died of operative complications. Of the 11 cases operated in that decade, 2 patients died as a consequence of liver necrosis, 2 as a result of hypovolemic shock, and 1 patient was found to have necrosis of the hepatojejunostomy at autopsy after developing cardiac arrest. Operative mortality between 1950 and 1969 was 15% (6 cases), owing to hypovolemic shock in 3 cases and to cardiopulmonary complications (massive pulmonary embolism, acute myocardial infarction, and cardiopulmonary arrest) in the remaining. Mortality decreased dramatically between 1970 and 1989. Only 12 operative deaths (4%) were observed in that period. Six patients (50%) died as a consequence of cardiopulmonary complications, 3 (25%) from hypovolemic shock, and 3 (25%) as a result of septic shock. Mortality decreased further to 1.5% in the most recent 2 decades. The predominant cause of death also changed: septic shock in 9 cases (33%). Less common causes included cardiopulmonary complications (acute respiratory distress syndrome, pulmonary embolism, and cardiac and respiratory arrest) in 26% of cases. Hypovolemic shock was seen in only 4 cases. The median time interval between operation and death was 20 days.

Complications—Pancreatic fistulae were the single most common complication (13%), followed by surgical wound infection, delayed gastric emptying, and intra-abdominal abscess (Table II). Biliary fistula and intra-abdominal bleeding were far less frequent (3% each). The rates of pancreatic fistula have remained relatively stable over time, reaching a peak in the 1950s when 20% of the patients developed this complication. Otherwise, the frequency of pancreatic fistula has remained between 9% and 13%. Intra-abdominal abscess also reached its peak in the 1950s (20%) and declined to a frequency of 3–13% over the next decades. In contrast, intra-abdominal bleeding was most frequent in the 1970s, when 1 of every 10 patients suffered this complication after a Whipple procedure. Its incidence has decreased markedly to <2% in the last 2 decades.

Reoperation—Sixty-nine patients required operative reintervention after the Whipple procedure, an overall reoperation rate of 3% (Fig 5, *D*). In the first 4 decades (up to 1985), the reoperation rate was 12%, and the single most frequent indication for reoperation was intra-abdominal abscess (37%), followed by intra-abdominal bleeding (25%). Some patients had multiple indications for reoperation, yielding a total of 82 indications (Table III). Of patients requiring reoperation, 18% died ultimately as a consequence of complications, and these deaths accounted for 42% of operative mortality in that early time period.

Since 1990, reoperation rates after a Whipple have been very low, an average rate of 2% (36 patients). The reasons prompting re-exploration have also changed. From 1990 to 2011, 53% were performed for intra-abdominal bleeding, whereas only 8% of reoperations were performed for an intra-abdominal abscess, likely owing to increased use of percutaneous drainage for this complication. Anastomosis revision, liver necrosis, wound reexplorations, and abdominal pain with negative exploratory laparotomy in 1 case comprised the rest of the interventions. The mortality of the reoperated patients was 22%. These deaths accounted for 30% of the operative mortality for the last 2 decades.

Duration of stay—The postoperative duration of stay after a Whipple procedure has decreased markedly over the decades (Fig 6, *A*). The average postoperative duration of hospital stay in the 1940s was 23 days. The actual hospital stay was substantially greater for those patients undergoing a 2-stage Whipple, who might spend months hospitalized. Hospital stay reached a peak between 1965 and 1974, when it was >30 days, but began decreasing in the 1980s, and continued to decline to the current stay of 9.5 days.

Readmission—Overall readmission rate for patients undergoing a Whipple procedure at MGH was 12% (244/2,050), intra-abdominal abscess being the most frequent reason (Table IV and Fig 6, *B*). Hospital readmissions after a Whipple remained infrequent for several decades. The low readmission rate seen over earlier decades corresponded with the greater hospital stay, ranging from 20 to 33 days on average. In the 1990s, however, parallel with earlier discharge at 14 days on average, the rate of readmissions increased to 9%. This trend continued after 2000, when readmission rates reached 15% as hospital stay declined to 9.7 days. The reasons for readmission did not show marked differences over the years.

DISCUSSION

The Whipple procedure in the 21st century has become a well-established operation that is performed with varying frequency throughout the world. A few medical centers in the United States, including the MGH, have become “high-volume” centers for pancreatic surgery. In these places, pancreatoduodenectomy, although still commanding respect as one of the most complex abdominal operations, is performed almost on a routine basis, many times per week. For the most part, patients come in with well-defined diagnoses and have cross-sectional imaging that show with great detail the anatomic relations between the pancreatic lesion that requires excision and the surrounding structures (including the vascular anatomy and its normal variants), allowing for adequate planning and a safe operation. The postoperative care is also very familiar to the surgeon, the residents, and the nursing staff, and because of all this, we walk a very comfortable path that almost always leads to success. History teaches us that this has not always been the case, and clearly our comfort level is the result of a gradual evolution from which we now benefit.

As best as can be ascertained, in our institution this evolution began in 1940, 5 years after Whipple presented his experience to the American Surgical Association. Over the next 30 years, the operation was done infrequently (on average, <2 cases per year), and the postoperative course was fraught with complications, including a likelihood of reoperation

of 10% and a mortality >20%. From 1970 to 1990, there was a 4-fold decrease in mortality (down to 5%), even though the reoperation rate (which in this and other series of pancreatoduodenectomy is generally associated with operative mortality^{8,9}) remained high (11%). This was the era when intensive care units were created,¹⁰ when general anesthesia became safer,¹¹ and, very importantly for pancreatic surgery, when computed tomography was incorporated into clinical care.¹² The latter not only allowed for earlier and more accurate preoperative diagnosis, but also for identification and management of complications. The earlier diagnosis of patients and the decrease in mortality were also likely driving forces for a modest increase in volume (mean of 13 cases per year).

The third era of pancreatoduodenectomy at the MGH encompasses the last 20 years, characterized by a steady increase in number of cases (mean of 39 per year between 1990 and 1994 to a mean of 144 per year between 2005 and 2011), a decrease in mortality to 1.7%, and a marked decrease in reoperation rates (2.1%). Although some of these improvements may still be related to better anesthesia and intensive care, most likely they are because of refinements in the operative technique and better management of complications. Many studies have correlated both individual and institutional operative volume to outcomes in pancreatic surgery and have been a driving force for regionalization of pancreatoduodenectomy and other complex operative procedures.^{13–16} At the MGH, the Whipple procedure went from being an uncommon operation done by many surgeons to a fairly common operation done by a handful of surgeons. The emergence and recognition of pancreatic surgery as a specialty contributed to this intra-institutional concentration, which in turn became a magnet for referral of patients, increasing volume, and better outcomes. It is impossible to pinpoint a particular element in operative technique or postoperative care that is responsible for the better outcomes, but like in any other human activity, “practice makes perfect,” and in turn the lessons learned from 1 surgeon permeate to others in the group. Whether it is use of closed-suction drains, fixed retractors with better exposure, a specific anastomotic technique, or a particular management of pancreatic leaks (to name a few) cannot be dissected out; however, the impact of a given individual can be inferred by analyzing the data. At the MGH, the driving force that converted the Whipple procedure to a safe and frequent operation was Dr Andrew Warshaw; he performed his first pancreatoduodenectomy as chief resident in 1971, joined the staff 1 year later, and rapidly became the “go-to” person for pancreatic problems. Between 1980 and 1999, Dr Warshaw performed 441 Whipple procedures, and in the same time period, 29 other surgeons performed 224. The comparison of outcomes is shown in Table V, and demonstrates how he became the transforming element in pancreatic surgery at the MGH.

In addition to the decisions made by the surgeon during the operation and postoperative care, the availability of interventional radiology at the MGH has also played an important role in the achievement of better outcomes, both to manage leaks and intra-abdominal abscesses, as well as postoperative bleeding.^{17–19} This great expertise, as well as that of the diagnostic radiologists, who have helped us identify patients and refine preoperative diagnosis, have fueled growth of the program, research opportunities, and better patient care.

Up until the discovery of vitamin K, the Whipple procedure was mostly a 2-stage enterprise because of the deleterious effects of high-grade biliary obstruction on coagulation. Currently, vitamin K is used rarely, and most patients with biliary obstruction come to operation after endoscopic or percutaneous drainage. The marked decrease in blood loss from the 1960s to the 1990s is multifactorial, but coagulopathy was a likely contributor. More impressive was the nearly universal use of blood replacement up to 1980, with a decrease to 15% in the more recent era. Analysis of this 7-decade experience also sheds light on other technical variations of pancreatoduodenectomy. Probably the most notable of this series was the common use of pylorus-preservation in the mid 1980s in the hopes that this

would have better nutritional outcomes in the long term. After our observation of an increased frequency of early delayed gastric emptying with this technique⁶ and a study also from our institution showing no long-term benefit,⁷ we abandoned its routine use and now use it only very selectively.

This experience also sheds light on the changes of the indication of the operation. Not unexpectedly, as pancreatoduodenectomy became safer, its indications expanded to include patients with benign disease, such as chronic pancreatitis in the 1980s, and in the last 2 decades both benign and premalignant cystic lesions, which are now the second most common indications for this operation. Although the data are not shown here, the indications have also expanded to include older patients and those with comorbidities that in the past would preclude such a high risk.

Finally, it is interesting to observe the patterns of duration of stay and readmission with pancreatoduodenectomy. The current mean duration of stay is one third less than what it was in the 1970s. As we have become more comfortable with the operation, we have challenged prior assumptions of oral intake and drain management from the past, and accelerate pathways that lead to early discharge. Clearly this approach has economic benefits for health care, and probably also for some patients who avoid morbidity simply from remaining in the hospital too long. This approach, however, has also led to an increase in the frequency of readmissions, which currently stand at 17%. Finding the right balance between early discharge and readmission remains an ongoing challenge.

It is unclear what lies ahead for pancreatoduodenectomy. Preventing complications and improving management of those that occur will of course continue to be a goal. Perhaps as we understand the natural history of pancreatic cystic lesions better, we will find that we do not need to operate on some of these patients, or alternative ways to treat them may be identified. The current trend to regionalization of pancreatoduodenectomy seems to have paid off in terms of decreased morbidity and mortality, but as more pancreatic surgeons are trained, some cases may go back to smaller hospitals. On the other extreme is the emergence of different operative approaches for the operation that would regionalize it even further. Development of laparoscopic surgery has reached the Whipple operation, and good outcomes in expert hands have been reported.^{20–22} The same is true for robotic-assisted pancreatoduodenectomy.^{23,24} Only time will tell if the open operation remains the standard in years to come.

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Fig 1.
Whipple procedures performed at the Massachusetts General Hospital between 1941 and 2011.

Indications for surgery

n = 2050

Fig 2.
Indications for Whipple procedure (1941–2011). *PDAC*, Pancreatic ductal adenocarcinoma.

Fig 3.
Operative reconstruction involved in the Whipple procedure. Drawn in a chart by house officer J.R. Newstedt, MD, in 1947.

Pylorus-preserving Whipple (PPW) and Delayed Gastric Emptying (DGE)

Fig 4.

Correlation between the proportion of pylorus-preserving Whipple procedures and the incidence of delayed gastric emptying as a complication.

Fig 5. Intraoperative variables and reoperation rates in 2,050 Whipple procedures. (A) Proportion of patients requiring intraoperative blood replacement. (B) Mean operative time for a Whipple procedure. (C) Operative mortality. (D) Reoperation rates.

Fig 6. Short-term surgical outcomes. (A) Mean duration of hospital stay over time. (B) Readmissions rate for operative complications.

Table IPostoperative deaths ($n = 50$)

Cause of death	<i>n</i>	%
Septic shock	12	24
Hypovolemic shock	12	24
Acute myocardial infarction	5	10
Pulmonary embolism	5	10
Massive upper gastrointestinal bleeding	4	8
Liver necrosis	4	8
Acute respiratory distress syndrome	2	4
Other	6	12

Table II

Complications

Complication	<i>n</i>	%
Pancreatic fistula	258	13
Biliary fistula	54	3
Wound infection	204	10
Delayed gastric emptying	193	9
Intra-abdominal abscess	155	8
Intra-abdominal bleeding	55	3

Table IIIIndications for reoperation ($n = 82$)

Indication	<i>n</i>	%
Intra-abdominal bleeding	22	27
Drainage of intra-abdominal abscess	17	21
Small bowel resection	7	9
Gastrectomy—bleeding gastric ulcers	3	4
Hematoma evacuation	3	4
Pancreatic fistula	2	2
Liver necrosis	2	2
Other	26	32

Table IVRe-admissions ($n = 244$)

Reason	<i>n</i>	%
Intra-abdominal abscess	50	20
Wound infection	20	8
Gastrointestinal bleeding	16	7
Delayed gastric emptying	14	6
Abdominal pain	12	5
Pancreatic fistula	11	5
Fever	11	5
Nausea/vomiting	10	4
Failure to thrive	10	4
Dehydration	9	4
Pneumonia	7	3
Other	74	30

Table V

Surgical outcomes for Whipple procedures between 1980 and 1999

	Dr Andrew L. Warshaw	Other surgeons (<i>n</i> = 29)		
	441	244	244	<i>P</i>
EBL (mean, SD)	881	40	1,180	86 .0018
Operative blood replacement (<i>n</i> , %)	105	24	102	42 .0001
Pancreatic fistula (<i>n</i> , %)	32	7	45	18 .0001
Intra-abdominal abscess (<i>n</i> , %)	11	2	17	7 .0085
Intra-abdominal bleeding (<i>n</i> , %)	6	1	10	4 .0447
Reoperation (<i>n</i> , %)	11	2	15	6 .0287
Surgical related death (<i>n</i> , %)	6	1	7	3 —

EBL, Estimated blood loss; *SD*, standard deviation.