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## Revolutionary transformation lowering the mortality of pancreaticoduodenectomy: a historical review

Bo Chang Wu<sup>1,2</sup>, Jakub Wlodarczyk<sup>1,3</sup>, Sanaz Nourmohammadi Abadchi<sup>1</sup>, Niloufar Shababi<sup>1</sup>, John L Cameron<sup>1</sup>, John W Harmon<sup>1</sup>

<sup>1</sup>Department of Surgery, Johns Hopkins School of Medicine, Baltimore, Maryland, USA

<sup>2</sup>Department of Surgery, University of Colorado Anschutz Medical Campus School of Medicine, Aurora, Colorado, USA

<sup>3</sup>Department of General and Oncological Surgery, Medical University of Lodz, Lodz, Poland

### Abstract

The History Maker paper focuses on the extraordinary revolution that dramatically improved the surgical results for the Whipple procedure (pancreaticoduodenectomy) in the 1980s and identifies Dr. Cameron as the leader of this revolution, who reported a mortality rate of approximately 1%. The revolutionary reduction of postoperative mortality for the Whipple procedure was achieved by adherence to gentle and precise Halstedian surgical techniques with adequate drainage of pancreatico-jejunal anastomosis with closed-suction silastic drains, along with the development of high-volume surgeons and hospitals. Excellent teamwork in patient care, including but not limited to preoperative evaluation by multidisciplinary teams, intraoperative communication between surgeons and anaesthesiologists, and postoperative management, contributed to a successful Whipple procedure.

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**Correspondence to** Dr Bo Chang Wu; bochang.wu@cuanschutz.edu.

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## INTRODUCTION

This History Maker article was written by the coauthors in collaboration with Dr. John Cameron. It is based on several, detailed discussions with Dr. Cameron in his office at Johns Hopkins Hospital and includes additional material gleaned from the scientific literature. The paper focuses on the extraordinary revolution that dramatically improved the surgical results for the Whipple procedure in the 1980s and identifies Dr. Cameron as the leader of this revolution.

Today, many medical centres are achieving the sort of excellent results which Dr. Cameron first consistently obtained. This fact is well documented in the USA and Europe. Dr. Cameron, who has served as Visiting Professor all around the world, notes that in China, Japan and India as well, there are centres that use high volume and other clinical approaches to achieve excellent results in pancreatic surgery.<sup>1</sup>

Surgeons trained by Dr. Cameron are leading high-volume centres in many parts of the USA and achieving excellent results. Notable among them are Charles Yeo at Jefferson, Keith Lillemoe at Massachusetts General, Chris Wolfgang at NYU, Richard Schulick at University of Colorado, Jeff Drebin at MSK, Henry Pitt at Rutgers, Herbert Zeh at UT Southwestern, Mike Zinner in Miami and others. Another of Dr. Cameron's trainees, Jin He, now leads the Johns Hopkins program, where he has pioneered the use of robotic surgery for the Whipple procedure.

At Johns Hopkins, the Cameron legacy continues with excellent, low postoperative mortality rates. Additionally, within the last 10 years, yet another dramatic change has taken place, namely, the introduction of even less invasive surgical techniques: the use not only of laparoscopic surgery, which is now wide-spread, but also of robotic surgery to perform the Whipple procedure.

## PANCREATODUODENECTOMY: THE WHIPPLE PROCEDURE

### The evolution of pancreaticoduodenectomy

The surgical treatment of periampullary tumours began at the end of the nineteenth century when two pioneers first operated on this type of cancer.<sup>2</sup> In February 1898, Dr. William Steward Halsted of Baltimore, Maryland, performed the first successful resection of a periampullary tumour with reanastomosis of the pancreatic and bile ducts.<sup>3</sup> The patient was discharged from the hospital but died from jaundice secondary to cancer recurrence a few months later.

The first successful regional resection of the pancreatic head with pancreaticoduodenostomy was performed by Dr. Walther Kausch in Germany in 1909.<sup>4</sup> Dr. Allen Oldfather Whipple from New York published three cases in 1935 and popularised the modern standard techniques for pancreaticoduodenectomy, which later became known as the Whipple procedure (figure 1).<sup>5</sup> By 1963, Dr. Whipple had performed 37 pancreaticoduodenectomies.<sup>2</sup> It was nonetheless around this time that the Whipple procedure was nearly abandoned because of a high in-hospital mortality of more than 25%.<sup>6</sup> The high in-hospital mortality

was thought to be related to several factors including the lack of experience of the low volume surgeons, the lack of well-established systems to address the postoperative complications such as sepsis and haemorrhage, and imprecise patient selection in the absence of advanced radiographic imaging.

### **Dr. John Cameron leading the revolutionary reduction in mortality of Whipple procedure**

A revolutionary transformation occurred in the 1980s when high-volume centres (defined as >25 cases per year) reduced in-hospital mortality to less than 5% (figure 2). A leader in this revolution was Dr. John Cameron of Johns Hopkins, who reported a mortality rate of approximately 1%.<sup>7</sup> He sought to concentrate on pancreatic cancer and dedicated his career to improving pancreatic surgery by lowering the mortality and morbidity associated with pancreaticoduodenectomy while increasing long-term survival. He performed over 2000 pancreaticoduodenectomies over the course of five decades and published a paper to document this milestone in 2014.<sup>7</sup> The first 1000 cases were performed over a period of 34 years, while the next 1000 cases were done within a period of 9 years. Dr. Cameron, who became known as the late 20th century's pioneer high-volume pancreatic surgeon, performed about 120–130 pancreaticoduodenectomies a year, with occasional stretches when he performed more than five Whipples a week. After Dr. Cameron reached the milestone of his two thousandth procedure, he went on to perform about 400 more pancreaticoduodenectomies. According to unpublished data, there was no difference in mortality between the first 400 and the final 400 cases, showing that the low mortality rate was the result of operative principles and procedures that did not change during the five decades.

According to Dr. Cameron, the origin of his success started in the 1890s when Dr. William Steward Halsted established the first surgery residency in the United States at the Johns Hopkins Hospital; where his surgical techniques, the Halstedian techniques, have been preserved and passed along to generations of students, residents and surgeons. Dr. Cameron emphasised that the Halstedian techniques, consisting of gentle tissue handling, excellent haemostasis, careful dissection and anastomosis (figure 3), were the key to keeping the Whipple procedure mortality rate low. He attributed his success to his adherence to the Halstedian technical principles. The main challenges that Dr. Cameron faced during 1970s were the unpredictability of postoperative bleeding, leak and infection. The operative techniques remained mostly unchanged, but he used the innovative closed-suction drainage during the operation to improve the Whipple procedure. Dr. Cameron pointed out that the placement of closed-suction drains right at the pancreatico-jejunal anastomosis (figure 4), replacing the previously used Penrose and cigarette drains greatly reduced the sepsis associated with pancreatic leaks.

### **High-volume centres**

But during the time of the revolution in outcomes, many factors played an important role in lowering the mortality and morbidity rates for pancreaticoduodenectomy. One was the appearance of the high-volume centres. Continuing experience in pancreatic operations resulted in lower perioperative mortality.<sup>8–12</sup> Not only did the surgeons become more adept with pancreaticoduodenectomy themselves, the residents, operating room nurses,

anaesthesiologists and the entire treatment team became more familiar with this operation and its associated complications, and more adept at managing complex problems that developed in the care of these patients. The Johns Hopkins Hospital reported a significant drop in perioperative mortality from 30% in the 1970s to 2% in the 1980s, which further decreased to 1% in the 1990s and 2000s.<sup>8,9</sup> Similarly, a dramatic decrease in perioperative mortality rate to 4% was also observed in another high-volume centre, the Massachusetts General Hospital in Boston, between 1970 and 1989.<sup>10</sup> The mortality rate further decreased to 1.5% in the 1990s and 2000s (figure 5).<sup>10</sup> Memorial Sloan-Kettering Cancer Center in New York has also reported a similarly low mortality rate since the 1980s.<sup>12</sup>

### **Advancement in imaging modalities**

Another key factor which significantly decreased negative outcomes of the Whipple procedure involved precise selection of patients. Before the advancement in cross-sectional imaging modalities, patients suspected to have pancreatic cancer would undergo an exploratory laparotomy for staging. Sometimes, when the disease had spread to the liver or other nearby structures and/or encased important vessels, patients were deemed not resectable. But other patients were resected under unfavourable circumstances. With the advent of CT in the late 1970s and MRI in the late 1980s and early 1990s, radiologists could delineate the anatomy and tumour involvement, helping surgeons decide if surgery should be offered and/or whether it could be safely done.<sup>13,14</sup>

### **Introduction of endoscopic retrograde cholangiopancreatography**

Another important advance was the introduction of endoscopic retrograde cholangiopancreatography (ERCP) to aid in diagnosis and preoperative preparation of patients with partial biliary obstruction.<sup>15</sup> This technique made it possible to palliate biliary obstruction by stent placement, preparing a patient for a future surgery or to cannulate the pancreatic duct after a conventional Whipple procedure.

### **Management of the postoperative complications**

Interestingly, the incidence of complications following a pancreaticoduodenectomy, such as anastomotic leak with sepsis, pancreatic fistula and pseudoaneurysm, has not markedly decreased over the last few decades.<sup>7</sup> It is the management of conditions that has changed. A closed-drainage system with suction has replaced the cigarette and Penrose drains, improving fluid drainage and further lowering the risk of infection. An additional important advance was the introduction of Interventional Radiology (IR). This allowed for drainage of abscesses complicating anastomotic leakage, thereby preventing or palliating associated complications, including intra-abdominal abscess formation, infection and sepsis. Before the era of IR, if a patient developed an abscess associated with anastomotic leak or a ruptured pseudoaneurysm with bleeding, an exploratory laparotomy to control the source of the infection or manage bleeding was indicated. Such an operation would disrupt the newly created anastomoses, resulting in high mortality. With IR, however, interventional radiologists can insert a drain with the fluoroscopic guidance.<sup>16</sup> IR also allowed bleeding from a pseudoaneurysm of the gastroduodenal artery to be managed quickly, appropriately and safely. Thanks to IR, pseudoaneurysms can now be occluded and addressed angiographically, with the main goal being to avoid reoperation. In addition, a

percutaneous biliary drain placed by an interventional radiologist can temporise obstructive jaundice until the patient receives definitive surgery.

### **Improvement in critical care**

In 1958, Peter Safar opened the first multidisciplinary intensive care unit (ICU) in Baltimore.<sup>17</sup> Since then, ICUs began to expand, allowing ever-sicker patients to be admitted and treated. During the period of the revolution in pancreatic surgery results, ICU care transitioned from part-time, minimally trained physicians to highly trained surgical intensivists with 24/7 inhouse coverage. At high-volume centres these intensivists learnt to recognise and treat surgical bleeding and anastomotic leaks early and effectively. Invasive monitoring systems, fluid administration, blood transfusions, oxygen administration and vasopressors became essential parts of the ICU, which allowed for more effective care of postoperative patients.

### **Other important pioneers in Whipple procedure**

In the late 20th century, there were many important figures along with Dr. Cameron who contributed to the improvement of results for hepato-pancreaticobiliary surgery. These include American surgeons Drs. Andrew Warshaw, John Braasch, Ken Warren, Murray Brennan, Howard Reber, Larry Way, Robert Hermann, Bernard Langer and others.<sup>18</sup> In Germany, Drs. Michael Trede and Markus Büchler achieved excellent postoperative outcomes.<sup>19</sup>

## **CONCLUSIONS**

The revolutionary reduction of postoperative mortality for the Whipple procedure was achieved by adherence to gentle and precise Halstedian surgical techniques with adequate drainage of pancreatico-jejunal anastomosis with closed-suction silastic drains, along with the development of high-volume surgeons and hospitals. Excellent teamwork in patient care, including but not limited to preoperative evaluation by multidisciplinary teams (surgery, gastroenterology, oncology, radiology), intraoperative communication between surgeons and anaesthesiologists and postoperative management (in the ICU, on the surgical floor and using IR), contributed to a successful pancreaticoduodenectomy or Whipple procedure (figure 3).

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

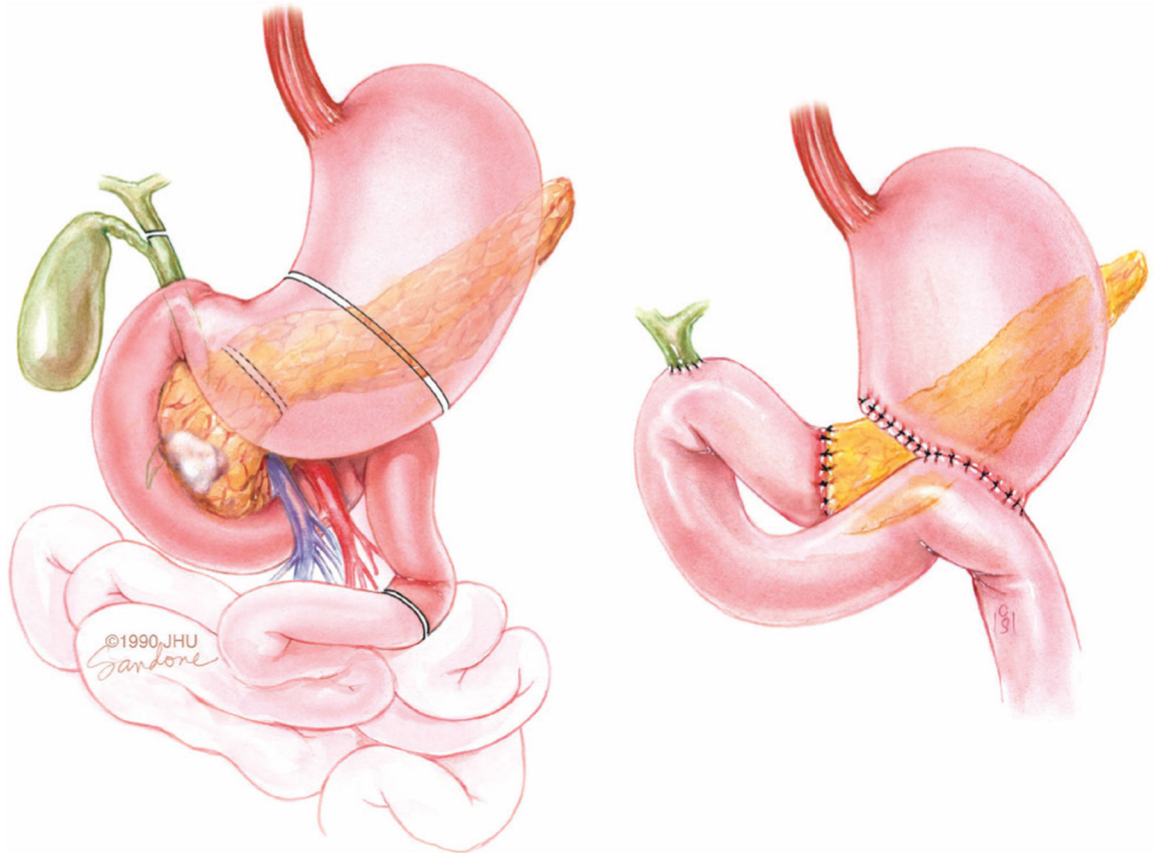
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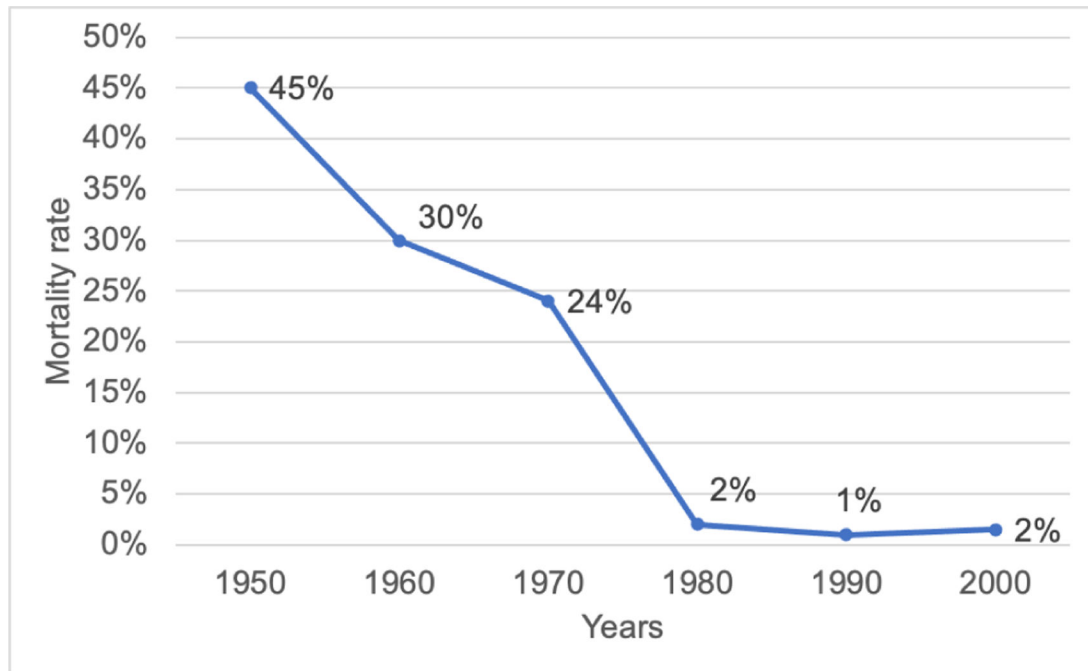
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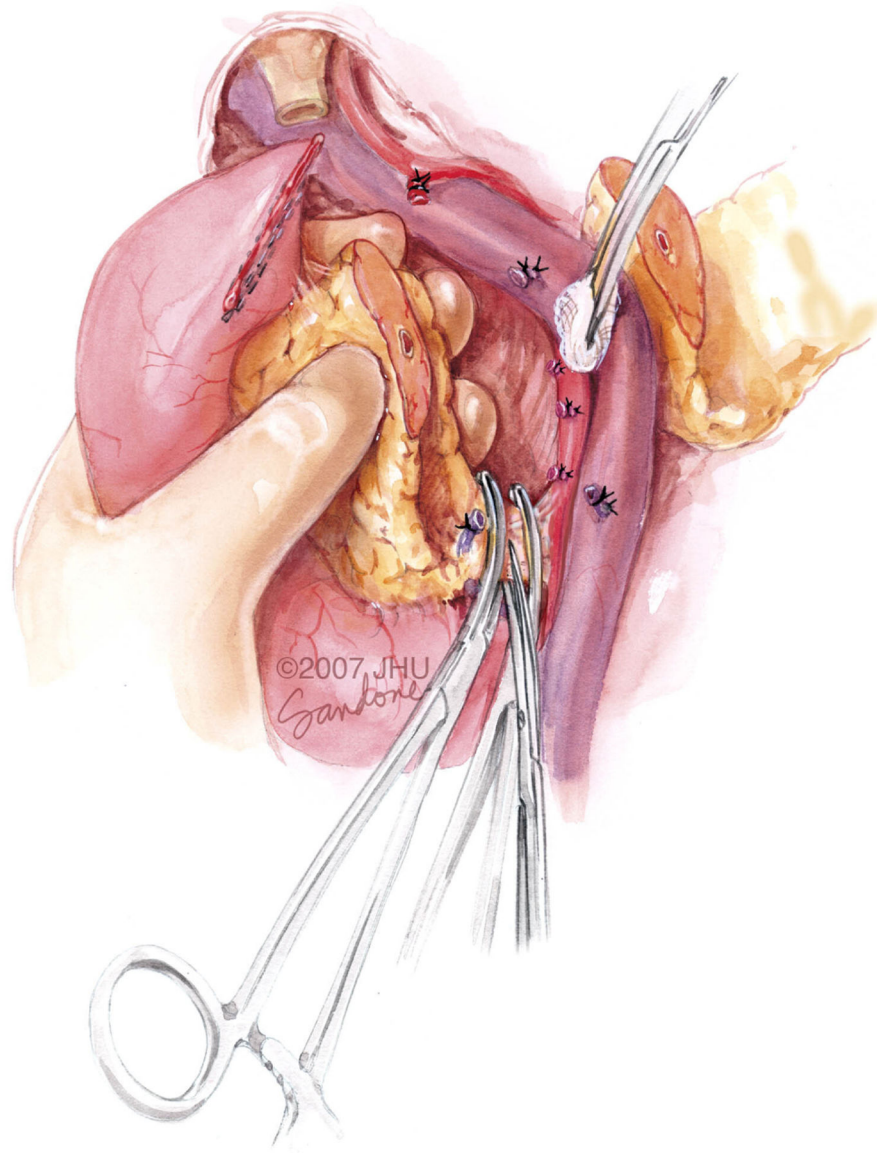
**Figure 1.** Illustration of the reconstruction before and after the Whipple procedure, pancreaticojejunostomy, choledochojejunostomy and gastrojejunostomy.<sup>20</sup> (Permission of reprint obtained (online supplemental file 1)).



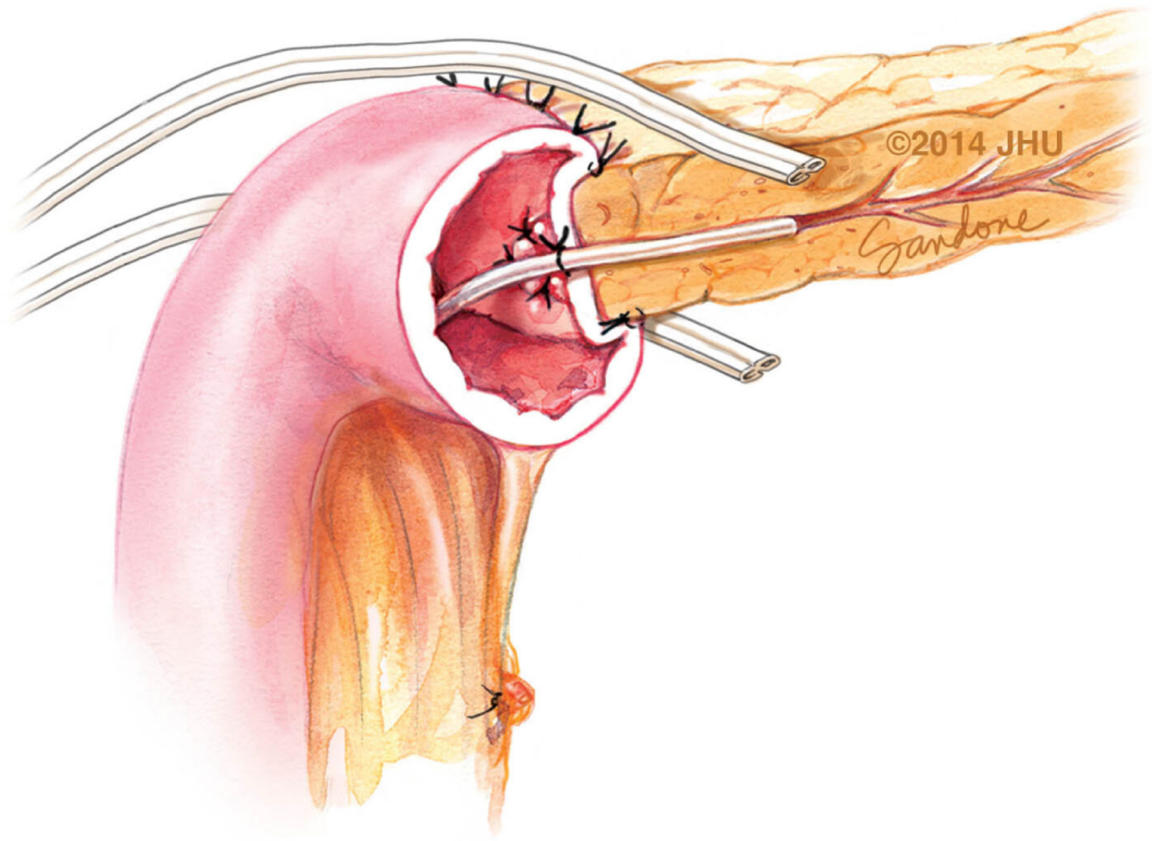
**Figure 2.**

Representing mortality rate after Whipple procedure over decades from 1950 to 2010. Data based on various references providing mortality rate after Whipple procedures performed in US hospitals from specific decades. In case of multiple data presenting specific decade mean value was provided. (References: 1950–1960s,<sup>10 21</sup> 1970s,<sup>22</sup> 1980s<sup>22</sup>, 1990s<sup>23</sup> and 2000s<sup>7</sup>).

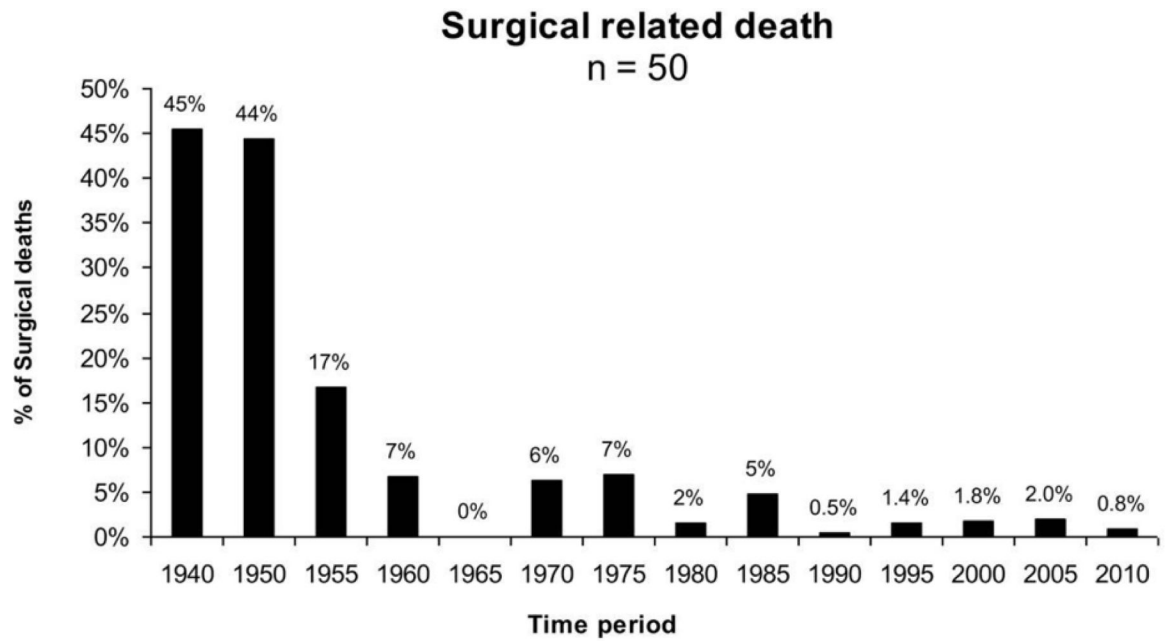




**Figure 3.** Careful dissection and gentle tissue handling during Whipple procedure.<sup>20</sup> (Permission of reprint obtained (online supplemental file 1)).



**Figure 4.** Placement of closed-suction drains at the pancreatico-jejunal anastomosis<sup>20</sup> (Permission of reprint obtained (online supplemental file 1)).



**Figure 5.**

Representing surgical-related death after Whipple procedure over time. Data recorded from Whipple procedures performed in Massachusetts General Hospital (Boston, Massachusetts, USA) between 1941 and 2011. n—number of postoperative deaths after Whipple procedure.<sup>10</sup> (Permission of reprint obtained).