

EDITORIAL

Pancreatic Cancer Surgery – What’s Next?

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The first reports on pancreatic cancer resections were published after operations performed by Friedrich Trendelenburg (Bonn) in 1882, Theodor Billroth (Wien) in 1884, Alessandro Codivilla (Imola/Bologna) and William S Halsted (Baltimore) in 1898, Walter Kausch (Berlin) in 1912, Georg Hirschel (Heidelberg) in 1914, and Alexander Brunschwig (Chicago) in 1937. Presumably, the majority of these operations were performed for cancers of the papilla of Vater rather than for exocrine pancreatic cancer. It wasn't until the publication by Allan Oldfather Whipple (New York) with two co-workers in 1935 [1] and subsequently his own article on "The rationale of radical surgery for cancer of the pancreas and ampullary region" in 1941 [2] that highlighted to surgical societies that pancreatic head cancer was technically resectable.

During his time in surgery Dr. Whipple only performed 37 "whipples", which in today's standards would classify AO Whipple as a "low-volume Whipple surgeon" The "Whipples" of today entail "resection of the pancreatic head" and in fact have little resemblance to the Whipple's original operations from 1935 with only slightly more resemblance to his later descriptions from 1941. Today, there is no optimal way of performing a "Whipple" and instead pancreatoduodenectomies may be performed in many different ways [3]. There have been no indications that one method is superior to another, and the optimum method is likely the one which the surgeon is most acquainted with.

The results of the surgery have progressed through several different stages since 1935 (**Table 1**), and the results are nowadays quite good even outside the centres of excellence in terms of the perioperative mortality [3, 4]. The long term results are still far from satisfying. Despite progressively more patients undergoing pancreatotomy for pancreatic adenocarcinoma – evaluated from 1992 to

2010 – with progressively smaller tumors and earlier stages of disease the longterm results have not improved. While it is true that patients lived longer (e.g. improved survival curves and median survival) but despite this, did not have an improved 5-year survival, denoting better early and intermediate survival [4]. However, the number of patients operated upon in 2010 – and even more so in 2018 – is far larger than in 1992. Meaning that this is a comparison of the fittest in 1992 with the fittest together combined with the not so fit as well as those with more advanced disease in 2010. Thus, the results are better from a population point of view despite the dissatisfaction of the statisticians. The improved result of surgery today is not due to one or a few new surgical technical innovations. Rather it is stepwise, gradual, and continuous progress based on improvements in radiology, anesthesiology, intensive care, oncology, nursing – and surgery. These disciplines in turn have progressed because of laboriously research, rather as a result of careful analysis of the large patient outcomes registries than of few Nobel-prize winning intellectuals. Our results of today stand on the shoulders of our surgical forefathers! If this is true, it is likely that today's results will be overthrown by tomorrows, and we will be able to say that our followers' results are based on our shoulders.

However, the young surgeons may not be satisfied with the present surgical outcomes – a dissatisfaction that sometimes may be shared with the generation that saw one fourth of all patients "whipped" never leaving the hospital alive when they started in surgery [5], and at their retirement met a postoperative mortality of 0-3 percent. At the turn of the last millennium the thought was that centralization of surgery should have an important

Table 1. The decades of pancreatic cancer surgery.

1940	Hurray, we can resect!
1950	Case reports
1960	Many hospitals
1970	Acceptable morbidity
1980	Acceptable mortality
1990	Centralization of surgery
2000	Adjuvants and neoadjuvants
2010	Focus on quality of life (with and without resection)
2020	Long-term survival?

Received January 28th, 2018 - Accepted January 30th, 2018

Keywords Pancreatoduodenectomy; Pancreatic Neoplasms

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Table 2. Predictions for pancreatic cancer surgery the next decade.

<i>Selection of patients</i>	<ul style="list-style-type: none"> - attempts on even more fragile patients - more strict selection for safe surgery - attempts on patients with limited liver metastases - routine of operations on overgrowth on large retropancreatic vessels
<i>Centralization of treatment</i>	<ul style="list-style-type: none"> - less centralization of “simple” cases due to better standardization pre-, per- and post-surgery
<i>Surgical technique</i>	<ul style="list-style-type: none"> - strict standardization of the surgical technique regarding for example lymph node resection - no more extended operations - possibly less invasive surgery in selected cases <ul style="list-style-type: none"> resection of more than one large retropancreatic vessel if needed - resection of local recurrences more often
<i>Adjuvant treatment</i>	<ul style="list-style-type: none"> - routine, probable more advanced but less toxic - (short-term) neoadjuvant treatment in most cases
<i>Other treatments</i>	<ul style="list-style-type: none"> - combinations with local treatments: by radiology, by local ablation therapy, etc
<i>Goals of treatment</i>	<ul style="list-style-type: none"> - safe surgery (complications not accepted as a part of surgery – the cause always possible to trace) - long-term quality of life acknowledged - cheaper surgery
<i>Research</i>	<ul style="list-style-type: none"> - patients get paid for participating in randomized trials - even larger, international high quality trials - trials combining surgery and molecular biology

impact on survival after resection for pancreatic cancer [6] – and while that was probably true – the benefits from that had probably already been achieved in most Western countries. There are likely other factors that now are more important for future progress in pancreatic cancer surgery (**Table 2**), and it must be appreciated that it is not *one* outstanding thought that will make the difference for the next set of patients with pancreatic cancer, but instead it is a cluster of small differences that together will ultimately increase long-term postoperative and oncologic survival.

Conflict of Interest

For non of the three authors exists a conflict of interests.

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