

# Does the textbook outcome in pancreatic surgery score after pancreaticoduodenectomy for ampullary carcinoma have prognostic value?

N Leech,<sup>1</sup> JEJ Krige,<sup>2</sup> S Sobnach,<sup>2</sup> JC Kloppers,<sup>1,2</sup> MM Bernon,<sup>2</sup> S Burmeister,<sup>2</sup> EG Jonas<sup>2</sup>

<sup>1</sup> Department of Surgery, Faculty of Health Sciences, University of Cape Town Health, South Africa

<sup>2</sup> Surgical Gastroenterology Unit, Groote Schuur Hospital, South Africa

Corresponding author, email: [nicholasbleech@gmail.com](mailto:nicholasbleech@gmail.com)

**Background:** The value of the textbook outcome in pancreatic surgery (TOPS) score, a composite measure of surgical performance for quality assurance, was evaluated in a South African tertiary hospital cohort of pancreaticoduodenectomies (PD) performed for adenocarcinoma of the ampulla of Vater (AAV).

**Method:** A review of all patients undergoing a PD for AAV at a single centre between January 1999 and December 2023 was performed. Demographic, operative, pathological and postoperative variables were recorded. Ten clinical and histological variables were used to construct a TOPS score. These included an R0 resection, no postoperative pancreatic fistula (POPF), no bile leak, no post-pancreatectomy haemorrhage, no delayed gastric emptying, no major postoperative complications (< Gr 3 Clavien-Dindo), no readmission to ICU, length of stay ≤ 10 days, no 30-day readmission or intervention and no 30-day mortality. A textbook outcome (TO) was defined as the fulfilment of all 10 variables. In patients in whom TO was not achieved, the reasons for failure were identified. In addition, the number of patients who had major complications and died were categorised as failure to rescue (FTR).

**Results:** A positive TOPS score was achieved in 27 of 79 (34.2%) patients undergoing a PD. Overall five-year survival after PD was 33.9%. TOPS conferred a significant 1-year survival benefit, 88.9% vs 66.7% (OR 4.12, 95% CI 1.08–15.67,  $p = 0.038$ ). There was no significant difference in 5-year survival between TOPS and non-TOPS patients, 40.0% vs 32.4% (OR 1.39, 95% CI 0.48–3.99,  $p = 0.54$ ). A POPF occurred in 31.6% patients, resulting in a significantly longer hospital admission, 17 vs 10 days (95% CI 2.66–11.34,  $p = 0.0019$ ). Twenty-one (26.6%) patients developed a major complication, five of whom died (FTR = 6.3%).

**Conclusion:** This study confirmed the value of TOPS as a useful measurement to assess hospital quality metrics and short-term survival after PD for AAV. One quarter of patients developed a major complication with a 6.3% FTR.

**Keywords:** ampullary carcinoma, pancreaticoduodenectomy, textbook outcome, morbidity, survival

## Introduction

Adenocarcinoma of the ampulla of Vater (AAV) is an uncommon histologically and molecularly heterogeneous tumour, accounting for 7% of periampullary and distal biliary malignancies and 0.2% of all gastrointestinal tumours.<sup>1</sup> True ampullary carcinomas have a more favourable prognosis than other periampullary malignancies with reported 5-year survival rates of 30–50% after pancreaticoduodenectomy (PD).<sup>1,2</sup> Although PD offers the best chance of cure, the long-term benefits should be balanced against the perioperative morbidity and mortality rates of a major pancreatic resection (PR). Postoperative mortality has decreased over the past decades to around 5% but postoperative morbidity remains substantial.<sup>3</sup> Assessment of the quality and outcome of specific operations has traditionally used discrete clinical and pathological indicators which have included postoperative morbidity, surgical margin status, and mortality. Evaluating each of these quality metrics in isolation does not, however, accurately reflect the total quality of a specific surgical operation and without standardised, clinically relevant and

universally applied endpoints, the evaluation of surgical interventions remains ill-defined and inconsistent.<sup>4</sup>

The development of the textbook outcome (TO) concept which reflects the ideal surgical outcome is a novel composite assessment based on a number of perioperative variables and is expressed as a binary endpoint.<sup>3,4</sup> The TO model evaluates the postoperative course in an all-or-none strategy in which the predefined “textbook outcome” is only considered met if each of the individual criteria is achieved. TO is increasingly used and has replaced previous quality of care scores. Efforts to standardise the definition and the components used in compiling a TO assessment have been variable as previous definitions have been arbitrary and tailored to be organ- or disease-specific.<sup>5</sup> Components used in compiling a TO in pancreatic surgery include the absence of a postoperative pancreatic fistula, bile leak, post-pancreatectomy bleeding, Clavien-Dindo ≥ III complications, and no 30-day readmission or in-hospital mortality.<sup>5</sup> Extended definitions have included duration of hospitalisation and the absence of resection margin involvement.<sup>5,6</sup>

The objective of the current study was to design a score based on previously described TO criteria but modified for relevance in AAV patients undergoing PD and assess its prognostic value. The secondary objective was to evaluate the FTR incidence in patients with major postoperative complications.

## Materials and methods

Consecutive patients with a histologically confirmed diagnosis of AAV who underwent a PD between January 1999 and December 2023 were identified from the pancreatic resection registry. Both the registry and this study were approved by the University of Cape Town Human Research Ethics Committee. Patients with pancreas, duodenum and distal bile duct tumours were excluded. Tumours were staged according to the 8th edition of the American Joint Committee on Cancer classification.<sup>7</sup> Data from 2017 onwards were retrieved from a prospectively maintained pancreatic resection database, data prior to 2017 were collected retrospectively via a folder review. Data collected included demographic information – age, gender, presenting symptoms, weight loss, body mass index, comorbidities – and biological and radiological data. Clinicopathological (degree of tumour differentiation, lymph node status, resection margin status) and operative data (duration of surgical procedure, blood loss, transfusion requirement) were recorded. All patients had preoperative routine blood tests and ultrasound or cross-sectional imaging (contrast-enhanced (CE-CT), magnetic resonance imaging (MRI) or both) and underwent endoscopic retrograde cholangiopancreatography (ERCP) including endoscopic biopsy, sphincterotomy and biliary stent insertion when appropriate. If endoscopic stenting was not technically possible, a percutaneous transhepatic cholangiogram with antegrade biliary stenting was performed. Mortality was defined as in-hospital death or death within 90 days of surgery.

## Textbook outcome

Ten clinical and histological variables were selected to construct a textbook outcome in pancreatic surgery (TOPS) relevant to AAV resection. These variables were chosen based on previous pancreatic surgery textbook outcome studies. The 10 variables were R0 resection, no pancreatic fistula, bile leak, or post-pancreatectomy haemorrhage, no delayed gastric emptying, no Clavien-Dindo post-resection complications  $\geq$  Gr III, a postoperative stay of 10 or less days, no readmission to ICU, and no hospital readmission or reintervention within 30 days, and no mortality within 30 days. A TO was defined as the fulfilment of all 10 variables. The reasons for TOPS failure were identified and the number of patients who had major complications and died were categorised as failure to rescue (FTR).

## Surgery

A pylorus-preserving pancreaticoduodenectomy (PPPD) was the resection of choice for AAV, performed by a board-certified hepato-pancreato-biliary (HPB) surgeon. During reconstruction, pancreatic duct stenting was performed in cases with small duct size ( $< 3$  mm) or soft pancreatic texture. A weighted nasojejunal feeding tube was placed during surgery and positioned 30 cm downstream from the

duodenojejunostomy in the efferent jejunal limb to allow early postoperative enteral nutrition.

## Pathology

The histological diagnosis of AAV was confirmed by an expert biliopancreatic pathologist. Resection margin (R) status was defined as follows: R0: tumour  $\geq 1$ mm from all resection margins, R1: tumour  $< 1$ mm from nearest margin, and R2: macroscopically involved margin. Histology reports were reviewed, and further oncological management discussed in a multidisciplinary meeting.

## Postoperative complication analysis

Postoperative complications were categorised according to the Clavien-Dindo classification.<sup>8</sup> Major morbidity was defined as Clavien-Dindo  $\geq$  grade III complications. Pancreatic surgery-specific complications (pancreatic fistula, post-pancreatectomy haemorrhage, delayed gastric emptying, bile leakage) were defined according to the International Study Group of Pancreatic Surgery and Liver Surgery criteria.<sup>9</sup> Patients with in-hospital mortality after development of a major complication (defined as Clavien-Dindo  $\geq$  III) were regarded as a failure to rescue (FTR). Post-pancreatectomy haemorrhage, bile leak and delayed gastric emptying (DGE) were defined according to the International Study Group of Pancreatic Surgery (ISGPS) definitions.<sup>10-12</sup> An unplanned return to theatre included any unplanned operation within 30 days of the index procedure. Peri- and postoperative mortality was defined as death during the initial hospital stay or at 30 days.

## Follow-up protocol

After resection, all patients were seen 3-monthly and a CT scan was done every 3 months during the first 2 years after surgery and every 6 months thereafter until 5 years. Tumour recurrence was diagnosed when a new lesion was shown on imaging or assumed if there were relevant signs or symptoms and a raised CA19-9. Long-term survival was calculated from death dates provided by the national census office.

## Outcomes

The primary outcomes assessed were TOPS, resection margin status, postoperative morbidity, FTR, 30-day mortality and long-term survival.

## Statistical analysis

Actuarial survival was calculated by the Kaplan Meier method. Categorical variables were presented as absolute numbers and percentage of patients and analysed using the  $\chi^2$  or the Fisher exact test. Continuous variables were expressed as mean  $\pm$  SD or median. Differences between the groups were analysed using the Mann-Whitney U test. The log rank test was used to determine the influence of TOPS on survival. A 2-tailed  $p$ -value  $< 0.05$  was considered statistically significant. Statistical analyses were performed using Stata, version 13 STATA 13 (StataCorp, College Station, TX, USA).

## Results

### Patient demographics and presentation

Seventy-nine patients (men 40, women 39, median age: 59 years, IQR: 51–66) were included in the study. Jaundice was the most common presenting symptom and significant weight loss was noted in most patients, while abdominal pain was an infrequent presenting symptom (Table I). Median duration of symptoms was 4 weeks (IQR, 3–6), and median delay from presentation to definitive resection was 5 weeks (IQR, 3–8). Forty-one patients (51.9%) had associated symptomatic cardiovascular disease, 12 had type 2 diabetes and three had a prior cholecystectomy. One patient in the cohort was HIV positive.

**Table I: Demographics and preoperative variables in 79 patients**

Variable	Ratio	
Sex (M:F)	40:39	
	<b>Median</b>	<b>IQR</b>
Age (years)	59	5–66
Duration of symptoms (weeks)	4	3–6
<b>Presenting symptoms</b>	<b>n</b>	<b>%</b>
Jaundice	74	93.7
Loss of weight	55	69.6
Pain	23	29.1
<b>Comorbidities</b>		
None	36	45.6
Hypertension	24	30.4
Diabetes mellitus	12	15.2
Ischaemic heart disease	5	6.3
Asthma	6	6.3
Previous biliary surgery	3	3.8
Previous cancer	3	3.8
Other	9	11.4

### Investigations

Seventy-five patients had a CT scan as part of the preoperative workup, two-thirds in combination with an ultrasound scan. Six (7.6%) patients had an MRI either in combination with or instead of a CE-CT scan. The median preoperative CA19-9 level was 84 (33–318). All but three patients underwent preoperative biliary drainage with endoscopic or percutaneous stenting. One patient had an endoscopic local excision of a pedunculated tumour to facilitate biliary stenting. Fifty-three patients had 10Fr 7 cm plastic stents inserted via ERCP, and nineteen had 10 mm self-expanding metal stents placed since 2017.

### Surgery and pathological variables

Seventy-eight patients underwent a PPPD, and one had a classic Whipple operation (Table II). An R0 resection margin was achieved in 91% of patients. The seven R1 resections were in patients with locally advanced tumours (pT4N1  $n = 3$ ; pT3N1  $n = 4$ ). R0 tumours were predominantly T2 (34.1%) and T3 (45.5%), two-thirds were histologically moderately differentiated and perineural, vascular and lymphatic invasion was present in 35%, 33% and 38% of

specimens, respectively. The median number of lymph nodes examined in the resected specimens was 9 (IQR 6–13) and nodal metastases were identified in 41 (51.9%) resections.

**Table II: Surgery and pathological variables**

Variables	n	%
<b>Operation</b>		
Classical pancreaticoduodenectomy	1	1.3
Pylorus-preserving pancreaticoduodenectomy	78	98.7
<b>Pancreatic anastomosis</b>		
Pancreaticojejunostomy	74	93.7
Pancreaticogastrostomy	5	6.3
<b>Resection margin involvement</b>		
R0	72	91
R1	7	9
<b>Pathological stage</b>		
T1N0	10	12.7
T1N1	1	1.3
T2N0	18	22.8
T2N1	9	11.3
T3N0	9	11.3
T3N1	27	34.2
T4N0	1	1.3
T4N1	4	5.1
	<b>Median</b>	<b>IQR</b>
Operation duration (minutes)	330	300–386
Blood loss (mls)	400	280–700
Number of nodes examined	9	6–13

### Textbook outcomes and postoperative complication

Twenty-one (26.6%) patients developed a major complication, five of whom died (6.3%) (Table III). One patient developed a POPF grade C complicated by intra-abdominal sepsis and died after a relook laparotomy. Four patients died postoperatively, one from the sequelae of a massive transfusion for intraoperative bleeding, the second after extensive small bowel ischaemia, the third after a pulmonary embolus and the fourth due to COVID pneumonia.

Thirty-six patients (45.6%) developed minor postoperative complications, the most common of which was surgical site infection (SSI) in 26 patients. Twenty-three (88.5%) patients with SSI were treated with antibiotics and wound care, while three (11.5%) required surgical intervention. Twenty-five patients (31.6%) developed a POPF of whom three (12.0%) required a repeat laparotomy, four (16.0%) were managed with percutaneous intervention, and 18 (72%) resolved on conservative management. A POPF grade B/C was more common in patients with major complications who were rescued than in those in whom rescue failed, but not statistically significant (84.6% vs 57.6%,  $p = 0.16$ ).

The median duration of hospitalisation was 11 days (IQR, 10–17). The median length of stay for the 23 surviving patients with a POPF was significantly longer than those without, 17 days in the POPF group vs 10 days in the no-POPF group (95% CI 2.66–11.34,  $p = 0.0019$ ). A TOPS was achieved in 27 (34.2%) patients. The most achieved TOPS

**Table III: Complications, grade, mortality and hospital stay**

Variable	n	%
<b>Complications frequency &gt; 10%</b>		
SSI	26	32.9
POPF A <sup>a</sup>	12	15.2
POPF B <sup>b</sup>	11	13.9
Ileus	8	10.1
None	22	27.8
<b>Clavien-Dindo grade</b>		
0	22	27.8
1	14	17.7
2	27	34.2
3a	5	6.3
3b	3	3.8
4a	2	2.5
4b	1	1.3
5	5	6.3
Early postoperative deaths	5	6.3
	<b>Median</b>	<b>IQR</b>
Length of hospital stay (days)	11	10–17

<sup>a</sup> – Post operative pancreatic fistula grade A, <sup>b</sup> – Postoperative pancreatic fistula grade B

parameters were ‘no post-pancreatectomy haemorrhage’ and ‘no bile leaks’, achieved in 77 (97.5%) patients, followed by ‘no mortality at 30 days’ in 74 (93.7%) patients. The least frequently met textbook outcome parameter was ‘length of hospital stay’ ≤ 10 days in 45 (43.0%) patients, followed by ‘no postoperative pancreatic fistula’ in 54 (68.3%) 79 patients. Twenty-one patients developed major complications (Clavien-Dindo ≥ grade III) – non-pancreatic complications in eight and POPF grades B and C in 11 and two patients respectively. In three of the 21 (14.3%) patients with major complications there was FTR.

**Survival**

The 1, 3, 5 and 10-year overall survival (OS) rates were 74.0%, 40.3%, 33.9% and 22.4% respectively and the 20-year OS in 21 patients who had surgery between 1999 and 2004 14.3%, two of whom are still alive, 21 and 23 years later. There was a statistically significant 1-year survival benefit for patients in whom a TOPS was achieved. One-year survival was 88.9% in the TOPS group and 66.7% in the non-TOPS group, (OR 4.12, 95% CI 1.08–15.67, *p* = 0.038) (Figure 1). However, there was no statistically significant difference in survival between the two groups at 3 and 5 years (Figure 2). The overall 5-year survival for N0 tumours was 57.6%. Median survival in N0 tumours was significantly longer than N1 tumours, 73 vs 28 months (95% CI 18.23–82.77, *p* = 0.0027). Five-year survival was 39.3%

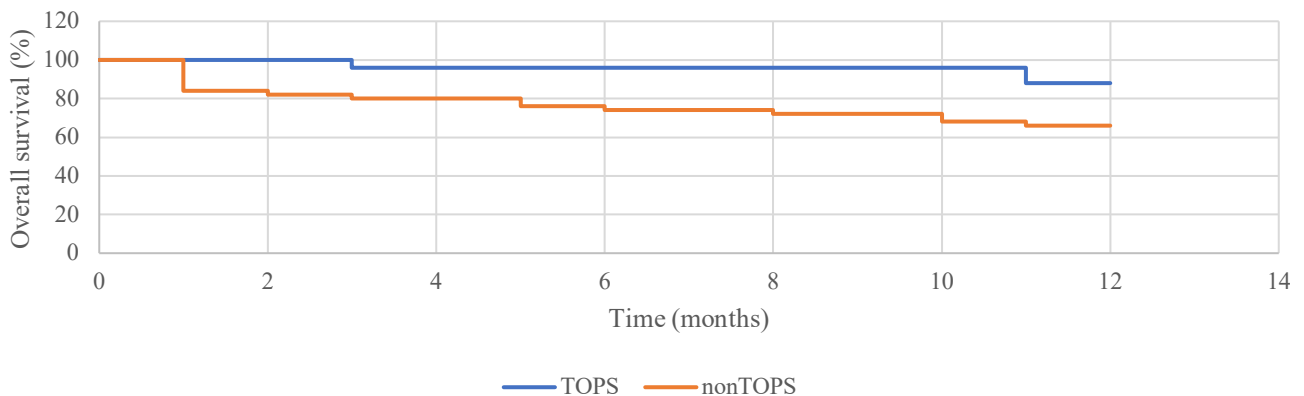


Figure 1: One-year survival after PD for AAV, TOPS (blue) vs non-TOPS (orange)

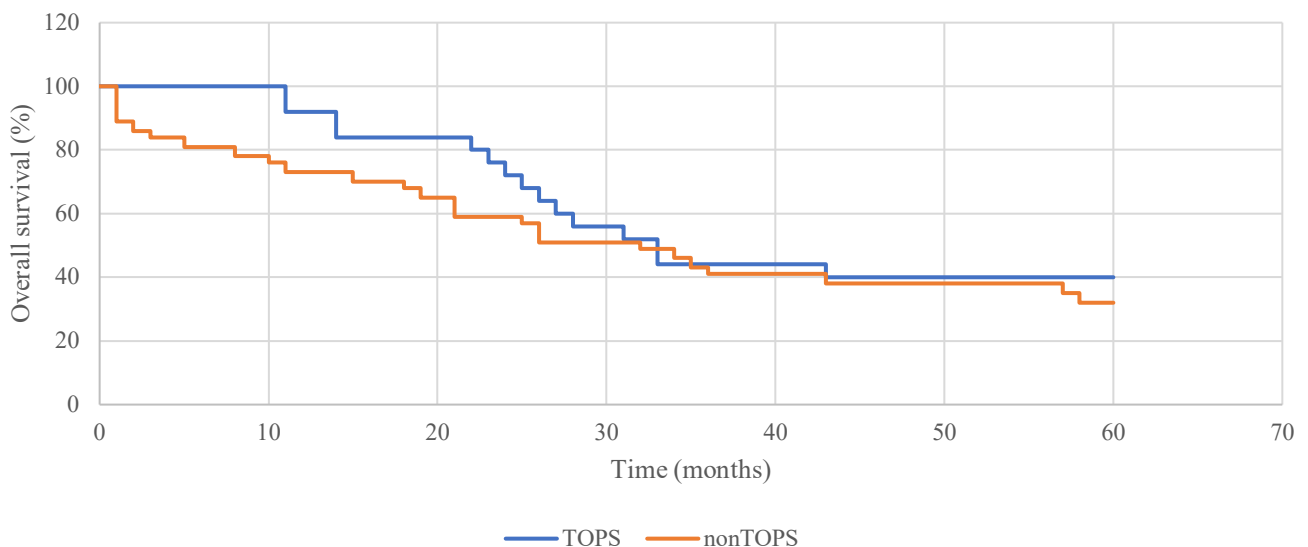


Figure 2: Five-year survival after PD for AAV, TOPS (blue) vs. non-TOPS (orange)

in the R0 resection group and 0% in the R1 resection group. Median survival in the R1 resection group was 18 months.

## Discussion

In this single centre observational study, we created a modified, expanded, ten component TOPS score, based upon previous pancreatic surgery textbook outcome scores, which was applied in a cohort of consecutive patients who underwent an elective PD for AAV. In addition, the study identified the reasons for TOPS failure and the number of patients with major complications in whom rescue failed. We found that an R0 resection was achieved in 91% of patients. Perineural, vascular and lymphatic invasion was present in one-third of patients while more than half had regional lymph node metastases. A quarter of patients developed major complications of whom three (6.3%) died. There was a steady decline in OS with 1, 3, 5 and 10-year survival rates of 74.0%, 40.3%, 33.9% and 22.4%. A TOPS score was achieved in 34.2% of patients. While there was a statistically significant 1-year survival benefit for TOPS patients, no significant difference in survival was found between the two groups at 3 and 5 years.

Several studies have provided data identifying a cohort of patients with AAV who are less likely to benefit from a pancreatic head resection.<sup>13-15</sup> Although radical surgery is curative in early-stage AAV, approximately half of patients will develop recurrence. Higher risks of relapse and worse clinical outcomes have been reported with poorly differentiated (G3) and locally advanced T3b and T4 tumours with ulceration, lymphovascular, perineural or venous invasion, lymph node metastases, positive resection margins, increased CEA and CA 19-9 levels, as well as molecular biological factors and patient factors such as age.<sup>13-16</sup> Patients with tumour involvement at the resection margin had a median survival of 12 months versus 60 months for those with negative resection margins.<sup>17</sup> The most important predictors of survival identified are positive lymph node status and lymph node ratios.<sup>18</sup> We found that stage of disease was the strongest predictor of survival, with significantly shorter survival in node-positive patients. The overall 5-year survival for N0 tumours was 57.6%. Our overall 5-year survival was 33.9%, which compares with published survival data ranging from 30–50%.<sup>1,2</sup> Achieving clear resection margins is crucial because 5-year survival was 39.3% after resection with tumour-free margins versus 0% in patients with involved margins, with a median survival of 18 months for the group with involved margins.

Quality assurance has become an important part of surgical practice and establishing standardised key metrics in patients who undergo complex procedures such as PD is crucial. Benchmarking is a quality improvement tool used to provide outcomes considered as reference standard for institutional comparisons.<sup>5,19</sup> Textbook outcome is not a new concept, having originally been described in colorectal oncological surgery, and has been posited as an ideal measure of the quality of surgical care as the formula incorporates a wide range of perioperative factors to provide a more comprehensive and holistic evaluation of surgical excellence.<sup>19,20</sup> However, the definition is arbitrary and heterogeneous across the surgical disciplines which provided the motivation for developing a pancreas-specific textbook outcome in this study. In addition to assessing short-term perioperative outcomes, achievement of an “optimal” TO

may also influence long-term survival. In the current study, we found that while achieving a TOPS score was associated with improved one-year survival, there paradoxically was no difference in 3- and 5-year survival.

Van Roessel et al. recognised the inconsistency in current TO descriptions and developed a score specific to pancreatic surgery for all indications based on a consensus survey.<sup>6</sup> Our TOPS score was developed to include all potential adverse events associated with PD for AAV. Resection margin status was included as this score is specifically designed for oncological pancreatic resections. It is important to consider that an R1 resection in our cohort exposed patients to a complicated postoperative course and shortened life-expectancy. Admittedly, these findings were not significant and require further validation.

An oncological resection variable that was not included in our score, or in the Van Roessel study, was number of lymph nodes resected. Positive lymph node status and lymph node ratio have been shown to be predictors of recurrence and long-term survival.<sup>2,18</sup> Zhang et al. included  $\geq 12$  lymph nodes examined, as per AJCC guidelines, in their textbook outcome definition when reviewing a cohort of patients that underwent PD for AAV between 1998 and 2020. The authors noted a discrepancy in the quality of lymphadenectomy, as the number of lymph nodes resected increased over time.<sup>5</sup> This may be due to an improvement in surgical techniques and will require validation in a larger sample if this finding is to be considered for inclusion in the further development of TOPS.

Mortality after the development of a major complication, designated as FTR, has also been used as a quality metric after pancreatectomy. However, comparisons of postoperative complications have historically been unreliable due to differing definitions of major complications or the description of FTR as death after any complication.<sup>21</sup> The risk factors for FTR after PD occurred more often in elderly patients with higher ASA scores and who had organ failure, life-threatening complications, shock and required reintubation postoperatively.<sup>21</sup> As a quality assurance metric, TOPS may be of more use, as there are multiple variables to target for improvement.

Our study has several limitations. Firstly, as the study was conducted in a single academic tertiary referral centre, the data accrual may have been affected by selection and treatment bias. Secondly, we used overall survival as the primary criterion to evaluate TO. A long procurement period was necessary to obtain five-year follow-up data for all the included patients and we acknowledge that surgical practice may have evolved during this time. Even with these limitations, this study provided robust data that allowed analysis and development of the TOPS score.

## Conclusion

In conclusion, surgical resection remains the mainstay of treatment for AAV. The results of this study support the role of PD in good-risk patients with AAV, with the anticipation of PR performed with curative intent, however overall long-term survival remains disappointing. Despite high resectability rates in AAV patients, the postoperative course is burdened by substantial complication rates. Our findings suggest that TOPS is a clinically relevant indicator and by increasing the existing number of TO components the TOPS score could provide a more detailed assessment of patient

outcome following PD for AAV. In addition, failure to rescue has been found to be an important additional outcome measure following PD for AAV.

### Conflict of interest

The authors declare no conflict of interest.








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### Ethical approval

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### ORCID

N Leech  <https://orcid.org/0009-0002-6973-8241>  
JEJ Krige  <https://orcid.org/0000-0002-7057-9156>  
S Sobnach  <https://orcid.org/0000-0002-4456-2115>  
JC Kloppers  <https://orcid.org/0000-0003-2438-6879>  
MM Bernon  <https://orcid.org/0000-0002-7967-8548>  
S Burmeister  <https://orcid.org/0000-0003-0888-7606>  
EG Jonas  <https://orcid.org/0000-0003-0123-256X>

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