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Long-term nationwide trends in the treatment of and outcomes among pancreatic cancer patients

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ABSTRACT

Whilst treatment modalities for pancreatic cancer patients have evolved in recent years, their impact on outcomes remains relatively unexamined on a national scale. We aimed to analyse changes in overall survival and trends in surgical and oncological treatments in pancreatic cancer patients diagnosed in the periods 2000 through 2008 and 2009 through 2016 in Finland. We collected data for pancreatic cancer patients diagnosed between 2000 and 2016, gathering data from the Finnish national registries on surgeries, oncological treatments and time of death. Follow-up continued through the end of 2018. We compared patients diagnosed between 2000 and 2008 to those diagnosed between 2009 through 2016. Our study comprised 14 712 pancreatic cancer patients. There was no significant change in the national resection rate (8.1% vs 8.0%, $p = 0.690$). In radical surgery patients, median survival improved from 20 months (95% confidence interval (CI) 18–22) to 28 months (CI 25–31) ($p < 0.001$), with 1-year survival ranging from 70% to 81%. In the no-surgery group, median survival slightly improved from 3.1 months (CI 3.0–3.3) to 3.3 months (CI 3.1–3.4) ($p < 0.001$). The proportion of radical surgery patients receiving preoperative oncological treatment increased from 4% to 13% ($p < 0.001$) and only postoperative treatment from 25% to 47% ($p < 0.001$). Whilst the resection rate did not increase, the prognosis of pancreatic cancer patients improved, particularly amongst radical surgery patients resulting most likely from the fact that a larger proportion of patients receive more effective oncological treatments.

1. Introduction

Finland has a population of 5.5 million and the public healthcare system cares for the large majority of pancreatic cancer patients, with no pancreatic surgery performed in the private sector. Finland has high-quality national registers providing comprehensive information about Finnish pancreatic cancer patients [1–3]. As a quality indicator of the Finnish Cancer Registry, in 2018 93.6% of all cancer cases were microscopically verified [2]. Reporting to the Finnish Cancer Registry is mandated by legislation.

In Finland, five university hospitals are situated in Helsinki, Turku, Tampere, Kuopio and Oulu. For each of these university hospitals, Finland is divided into five specific catchment areas which are further divided into a total of 21 healthcare districts. The centralisation of pancreatic surgery has reportedly improved resection rates and survival [4,5]. Although some trend towards the centralisation of pancreatic cancer surgery to Finland's five university hospitals has emerged during the 2000s the legislation was not enacted until 2018. Pancreatic cancer is a gastrointestinal malignancy with an especially poor prognosis [6,7]. The annual incidence of pancreatic cancer in Finland has increased from 19 per 100 000 in 2000 to 24 per 100 000 in 2016, which is high compared to estimates for the European incidence of 10 per 100 000 [8,9]. Pancreatic cancer is most often diagnosed at an advanced stage partially due to late presenting symptoms [10]. Overall prognosis remains poor, although minor improvements have been reported in population-based studies [6,11]. In the global Concord-3 register study, the 5-year survival of Finnish pancreatic cancer patients

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Abbreviations

95% confidence interval CI
International Classification of Diseases Version 10 ICD-10
Care Register for Health Care HILMO
Year y
Median Mdn
Hazard ratio HR
Charlson Comorbidity Index CCI
Pancreaticoduodenectomy PD
Distal pancreatic resection DPR
Total pancreatectomy TP

improved from 4.1% in 2000–2004 to 7.4% in 2010–2014 [6]. Radical resection, as a part of multimodal therapy, represents the only known potentially curative treatment [12].

The aim of this study was to investigate changes in the treatment of and survival amongst pancreatic cancer patients in Finland between 2000 and 2016. The hypothesis was that the proportion of patients undergoing radical intent treatment would have increased and survival would have improved due to advancements in the treatment of pancreatic cancer in recent decades [12–15]. Neoadjuvant therapy plays an increasing role in the treatment of borderline and particularly locally advanced cases [13,14,16–18].

2. Material and methods

Patients diagnosed with pancreatic cancer (ICD-10 code: C25) between 2000 and 2016 were identified from the Finnish Cancer Registry. In 71% of patients, data on stage was available in the registry but as it was inconsistently classified and has been reported to be partly unreliable, it was not included in the analysis [19]. Residence as well as time and cause of death were collected from Statistics Finland. Patients' healthcare visits were collected from the Care Register for Health Care (HILMO) from the National Institute for Health and Welfare. The Care Register includes nationwide data on patients discharged from inpatient care, day surgeries and specialised outpatient care. The completeness of the source data has been evaluated to be excellent especially regarding inpatient data and thus data on pancreatic surgeries [1]. Treatment periods including surgery were identified based on the Nordic Classification of Surgical Procedures. Charlson comorbidity index (CCI) was collected based on healthcare visits prior to pancreatic cancer diagnosis [20–22]. Patients with a diagnosis of a neuroendocrine tumour (ICD-10 code C25.4) or pancreatic tumour enucleation procedure were excluded (n = 189). Patients younger than 18 years old at diagnosis were excluded (n = 3). Cases in which the method of diagnosis was death certificate only (n = 740) or autopsy (n = 1781) were excluded since the duration of survival is unknown [23].

To investigate changes in treatment and survival, we divided patients into two groups based on the period during which they received their diagnosis: 2000–2008 and 2009–2016. We calculated overall survival, and censored patients still living as of 31 December 2018.

Radical surgeries consisted of pancreaticoduodenectomy, distal pancreatic resection, total pancreatomy and unspecified pancreatic resections. In our analysis, we grouped open and minimally invasive operations together. Postoperative mortality was calculated at 30 days and at 90 days following surgery. Patients undergoing elective explorative or biliodigestive bypass procedures, but not radical pancreatic surgery, were identified as representing a patient group treated with radical intent but were identified as non-resectable. We labelled this group as diagnostic surgeries. On-call procedures were not included.

Chemo- and radiation therapy were identified from the HILMO data for the pancreatic cancer treatment periods using oncological treatment procedure codes (Nordic Classification of Surgical Procedures). Whilst the coverage of oncological treatment data in HILMO was unknown, we collected local patient register data from the Helsinki University Central Hospital area and compared the two datasets. It was found that 85% of patients who had oncological treatment based on the local register data had it also based on the HILMO data. Datasets were then combined. By comparing the dates of the oncological treatments and that for surgery, we determined whether the oncological treatment was only preoperative, only postoperative or perioperative for patients that underwent surgery. Information about specific chemotherapy agents was not available.

Data were analysed in three groups based on the surgical treatment: radical surgery, diagnostic surgery and no surgery. Based on the oncological treatment, we further divided the data into the following subgroups: perioperative, only preoperative, only postoperative and no oncological treatment in the radical surgery group; preoperative, only postoperative and no oncological treatment in the diagnostic surgery group; and any and no oncological treatment in the no-surgery group.

In this study, patients were divided into the specific catchment areas, Helsinki, Turku, Tampere, Kuopio and Oulu, according to their home municipality during the year of their diagnosis. We then compared regional differences between these five specific catchment areas.

We performed all statistical analyses using IBM's SPSS Statistics for Windows, version 27.0.1 (Armonk, NY: IBM Corp). Changes in treatment groups were evaluated using the Fisher's exact test or the chi-square test. Survival amongst different groups was analysed using the Kaplan-Meier method, whereby we compared differences using the log-rank test. The Bonferroni method was used for multiple comparisons requiring adjusted p-values.

Cox regression was used for a multivariate analysis of radically operated patients. In 112 patients the delay of starting postoperative oncological treatment after radical surgery was more the 6 months and this was thought to represent palliative treatment of recurrent disease. These patients were censored at 6 months from radical surgery in the multivariable analysis. Six patients were excluded for the multivariate analysis because they had preoperative oncological therapy started over 12 months before the radical operation. Immortal time bias was corrected for oncological treatments by using time dependent variables to classify the patients to different oncological treatment groups in timely manner. For neoadjuvant treatment group the time of classification was at surgery date and for the adjuvant group the beginning of the adjuvant treatment. In patients undergoing perioperative treatment, we estimated the period from surgery to adjuvant treatment from the adjuvant treatment group (median time). Since the cox assumption of constant hazard ratio (HR) over time was not fulfilled for adjuvant and perioperative treatments, a time dependent variable was added. Interactions were considered, but no significant interaction were found after Bonferroni correction for multiple testing. The follow-up time was restricted to nine years for the cox regression analyses. We considered $p < 0.05$ statistically significant applying two-tailed tests.

The National Institute for Health and Welfare (THL/1255/5.05.00/2018), Statistics Finland (TK-52-832-19) and the Helsinki University Hospital (§ 91 HUS/419/2018) approved the study protocol.

3. Results

In total, our study comprised 14 712 patients, amongst whom 6903 (47%) were male and 7809 (53%) female (Table 1). The median age was 73 years (range 19–103). There were 6702 (46%) patients diagnosed in 2000–2008 and 8010 (54%) patients diagnosed in 2009–2016. The median age for each period was 73 (range 21–103) and 73 (range 19–102) years, respectively. The distribution of patients across specific catchment areas was as follows: 4740 (32%) patients in Helsinki, 2985 (20%) in Tampere, 2507 (17%) in Turku, 2359 (16%) in Kuopio and 2045 (14%) in Oulu.

Method of diagnosis was histology of primary tumour or metastasis in 47% (n = 4967), cytology in 14% (n = 14) and clinical, including radiological imaging and specific tumour markers in 39% (n = 5720). In 99% (n = 1066) of patients who underwent radical surgery, the diagnosis was confirmed by histology. Comparing 2000–2008 and 2009–2016 there were 1132 vs 649 cases diagnosed with autopsy ($p < 0.001$) and 402 vs 338 patients with death certificate only ($p < 0.001$) that were excluded from further analyses.

Comparing the time periods 2000–2008 and 2009–2016 by the Charlson comorbidity index at the time of diagnosis, there were 60% (n = 4010) vs 43% (n = 3431) patients with a score of 0, 20% (n = 1319) vs 22% (n = 1742) with a score of 1, 12% (n = 822) vs 17% (n = 1381) with a score of 2 and 8% (n = 551) vs 18% (n = 1456) with a score of 3 or more, $p < 0.001$. In the radical surgery group, there were 68% (n = 369) vs 51% (n = 326) with a score of 0, 19% (n = 103) vs 20% (n = 125) with a score of 1, 9% (n = 50) vs 17% (107) with a score of 2 and 4% (n = 23) vs 12% (n = 79) with a score of 3 or more, $p < 0.001$. Prevalence of specific comorbidities among patients at the time of diagnosis is provided in the Supplementary Table 1.

A total of 1182 (8.0%) patients underwent radical surgery for pancreatic cancer. Radical surgeries consisted of pancreaticoduodenectomy in 951 (81%) patients, distal pancreatic resection in 145 (12%), total pancreatectomy in 65 (6%) and unspecified pancreatic resection in 21 (2%). Annual resection rate ranged from 6.3% (n = 47) in 2004 to 11.4% (n = 120) in 2016. We detected no significant change in the resection rate for any region when comparing the time periods 2000–2008 and 2009–2016.

In the radical surgery group, 30-day mortality was 1.9% (n = 22) and climbing to 3.3% (n = 39) for 90-day mortality. The 30-day mortality did not significantly change, from 1.7% (n = 9) in 2000–2008 and 2.0% (n = 13) in 2009–2016 ($p = 0.671$). The 90-day mortality also did not significantly change, reaching 3.5% (n = 19) in 2000–2008 falling to 3.1% (n = 20) in 2009–2016 ($p = 0.740$).

In diagnostic surgery group, 42% (n = 235) vs 42% (n = 131) patients underwent elective biliodigestive bypass and 58% (n = 325) vs 58% (n = 184) only elective explorative surgery. There were 12 676 patients (86%) who did not undergo elective surgery for pancreatic cancer.

A total of 3257 (21%) patients received oncological treatment for pancreatic cancer. Twenty percent (n = 3001) received chemotherapy and 3.3% (n = 486) radiation. Comparing 2000–2008 and 2009–2016, we observed a significant increase in the proportions receiving oncological treatment from 13% (n = 848) to 29% (n = 2286) ($p < 0.001$). Likewise, there were significant increases in the proportions of patients receiving chemotherapy (12% vs 27%, $p < 0.001$) and radiation (1.6% vs 4.7%, $p < 0.001$).

In the radical surgery group, the proportion of patients receiving oncologic treatment increased from 30% (n = 162) to 60% (n = 385) (Table 1). Amongst patients who received preoperative treatment before radical surgery (n = 109), 79% (n = 86) also received postoperative treatment. In the radical surgery group, 8% (n = 96) of patients received radiation therapy. Overall, 13% (n = 56) of those undergoing only postoperative treatment and 37% (n = 40) of patients receiving preoperative chemotherapy also received radiation therapy.

The median overall survival across all patients improved from 4.0 (CI 3.9–4.2) to 4.2 (4.0–4.4) months ($p < 0.001$). Table 2 summarises the overall survival amongst treatment groups. The Kaplan–Meier survival plot for the radical surgery group comparing 2000–2008 and 2009–2016 appears in Fig. 1. In the radical surgery group, patients receiving only preoperative treatment (n = 23) versus pre- and postoperative treatment (n = 86) revealed overall survival of 25 (CI 12–39) versus 36 (CI 30–41) months ($p = 0.158$).

In the non-surgical group, we found a minor improvement in the median survival from 3.1 months (CI 3.0–3.3) to 3.3 months (CI 3.2–3.5) ($p < 0.001$). In the no-surgery group, the median survival for patients receiving oncological treatments (n = 2324) versus patients who did not receive treatment (n = 10352) was 9.2 (CI 8.8–9.6) versus 2.4 (CI 2.3–2.5) months ($p < 0.001$).

Cox regression analysis of effects of clinical parameters on overall survival in patients undergoing radical resection is presented in Table 3. Multivariate analysis was adjusted for age, sex, Charlson comorbidity index, catchment area and operation type. After adjustments, the improvement in survival over time between the inspected time periods 2000–2008 and 2009–2016 was clearly observable (HR 0.68, $p < 0.001$), as well as the initial effect of postoperative adjuvant treatment (HR 0.74, $p = 0.027$) and perioperative adjuvant treatment (HR 0.52, $p = 0.016$). Only 21 patients received solely neoadjuvant treatment, and it did not reach significance. Patients treated in the Helsinki catchment area had

Table 1
Surgical and oncological treatments among Finnish pancreatic cancer patients in 2000–2008 and 2009–2016.

		2000–2008			2009–2016			
Surgery	Oncological treatment	N	(%)*	Age**	n	(%)	Age	p***
Radical		545	(8)	66	637	(8)	67	1.000
	Perioperative	10	(2)	63	76	(12)	65	<0.001
	Only preoperative	14	(3)	64	9	(1)	66	1.000
	Only postoperative	138	(25)	64	300	(47)	67	<0.001
	None	383	(70)	67	252	(40)	67	<0.001
Diagnostic		545	(8)	66	309	(4)	68	<0.001
	Preoperative	9	(2)	60	23	(7)	64	0.423
	Only postoperative	122	(22)	64	109	(35)	67	0.234
	None	414	(76)	67	177	(57)	68	<0.001
None		6702	(84)	74	8010	(88)	74	<0.001
	Any	555	(10)	64	1769	(25)	68	<0.001
	None	5057	(90)	75	5295	(75)	77	<0.001

*percentage within each group, **median age, *** the change in treatment group proportion 2000–2008 vs 2009–2016.

Table 2
Overall survival among Finnish pancreatic cancer patients diagnosed in 2000–2008 and 2009–2016 grouped by surgical and oncological care received.

	Oncological	2000-08 Survival					2009-16 Survival					
Surgery	treatment	1y	3y	5y	Mdn	(95%CI)	1y	3y	5y	Mdn	(95%CI)	p*
Radical		0.68	0.27	0.16	20	(18–22)	0.79	0.39	0.26	28	(25–31)	<0.001
	Perioperative	0.90	0.40	0.30	16	(0–45)	0.91	0.51	0.31	36	(30–42)	1.000
	Only preoperative	0.79	0.36	0.36	31	(24–37)	0.67	0.11	0.11	20	(31–41)	1.000
	Only postoperative	0.83	0.38	0.16	30	(25–34)	0.87	0.44	0.29	31	(26–35)	0.234
	None	0.65	0.24	0.16	17	(15–20)	0.71	0.33	0.23	22	(16–24)	0.139
Diagnostic		0.33	0.03	0.01	8	(8–9)	0.35	0.03	0.02	9	(8–10)	0.105
	Preoperative	0.78	0.00	0.00	15	(14–16)	0.74	0.04	0.00	17	(13–20)	1.000
	Only postoperative	0.52	0.06	0.03	12	(11–13)	0.45	0.06	0.04	12	(10–12)	1.000
	None	0.27	0.02	0.01	7	(6–8)	0.25	0.02	0.01	7	(6–8)	1.000
None		0.13	0.03	0.02	3	(3-3)	0.17	0.05	0.03	3	(3-3)	<0.001
	Any	0.40	0.10	0.05	10	(9–11)	0.37	0.09	0.05	9	(9-9)	1.000
	None	0.13	0.03	0.02	3	(3-3)	0.13	0.04	0.03	2	(2-2)	0.020

Abbreviations: y, year; Mdn, median in months; *Log-rank test P value for 2000–2008 vs 2009–2016.

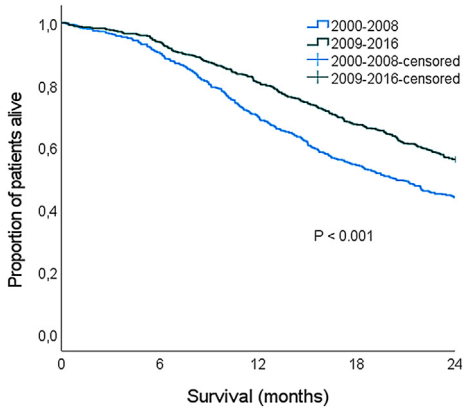

Fig. 1. Comparison of overall survival among radical surgery pancreatic cancer patients diagnosed in 2000–2008 and 2009–2016 in Finland.

better survival compared to the other catchment areas.

4. Discussion

In this nationwide longitudinal study of 14 712 pancreatic cancer patients over 17 years, survival improved, particularly amongst patients undergoing radical surgery. Although the proportion of patients who underwent diagnostic surgery decreased, possibly indicating a better preoperative evaluation and the improved detection of non-resectable disease, the national radical resection rate remained steady at 8%. Low resection rate may indicate stricter patient selection, supported by our results of good survival outcomes. Although the excluded proportion of patients diagnosed post-mortem decreased from 2000 to 2008 to 2009–2016 the size of the cohort was still substantial. Reported resection rates in the US and other European countries range from 8% to 21% in population-based studies [11,24–26]. Finland has a comparably high incidence for pancreatic cancer which might indicate a better coverage of palliative-treated patients in registers compared to population-based registries in other [7–9]. However, trends towards increasing resection rates have been reported in population-based studies in the US, Denmark, the Netherlands and in France yet, no increase was observed in Belgium, Norway, Slovenia or Estonia [11,24,26]. In another Finnish study, the resection rate reportedly varied between the 21 healthcare districts ranging from 7.7% to 17.9% in 2003 and 2008 [5]. In that study, patients were selected from the Finnish cancer registry, but many were excluded based on missing patient records possibly explaining higher observed resection rates. Regional differences in the treatment of pancreatic cancer in Finland were also observed in our study as patients treated in Helsinki catchment area had a survival advantage in the multivariable analysis. In this catchment area, all pancreatic surgery is performed in a single high-volume centre, the Helsinki University Hospital, in recent years.

Increased rates of both preoperative and postoperative oncological treatments are a potential explanation for improved survival amongst those undergoing radical surgery. However, patients diagnosed in 2009–2016 had a significant independent survival advantage in the multivariate analysis. Patients who received postoperative oncological treatment in addition to preoperative treatment exhibited promising survival rates in our study although this may have been influenced by a selection bias. In a recent retrospective cohort study adjuvant therapy improved survival after neoadjuvant treatment only in patients who had a node positive disease [27]. Neoadjuvant therapy has been reported to carry a survival advantage compared to upfront surgery particularly for higher stage and grade-three tumors [14,28,29]. In the US, the neoadjuvant therapy rate for patients with stage I or II disease reached 7.5% overall, which increased from 4.3% to 17% between 1998 and 2011 [30].

An increased rate of oncological therapy in the no-surgery group most likely explains the minor improvements to survival. Van der Geest reported similar overall survival amongst palliative patients in the Netherlands, reporting an overall survival of 7 weeks in untreated patients and 25 weeks in patients receiving chemotherapy [31]. Increasing rates of oncological treatments for palliative patients were reported in the European Union. Specifically, Nienhuijs et al. reported an increase in the palliative chemotherapy rates amongst nonsurgical patients from 5% to 19% in the Netherlands [11]. In another nationwide Dutch study, systemic palliative therapy doubled between 2005 and 2013 [31]. In a smaller French register study from the Finistère Area, the palliative chemotherapy rate was much higher at 45.6% [26].

The strengths of this study include its reliance on a comprehensive long-term nationwide dataset for pancreatic cancer patients which combined information from oncological and surgical treatments. Furthermore, we relied on a large sample size with excellent coverage of the Finnish population. Finally, our data were collected from high-quality registers [1,2].

The limitations of this study include the secondary nature of register data. A substantial proportion of cases were diagnosed post-mortem and were removed from further analysis since duration of survival is unknown. Further, exclusion of autopsy and death certificate only cases is recommended in data quality control for cancer survival studies [23]. The rates for patients receiving

Table 3
Multivariable analysis of effects of clinical parameters on overall survival in pancreatic cancer patients undergoing radical resection.

Parameter	Univariate	95% CI			Multivariate	95% CI		
	HR	lower	upper	p	HR	lower	upper	p
Age at diagnosis								
Years	1.02	1.01	1.02	<0.001	1.02	1.01	1.02	<0.001
Gender								
Male	1.00				1.00			
Female	1.03	0.90	1.18	0.705	1.02	0.89	1.18	0.745
CCI								
0	1.00				1.00			
1	0.94	0.78	1.12	0.475	0.93	0.77	1.12	0.436
2	0.93	0.75	1.14	0.457	0.91	0.74	1.13	0.384
3 or more	1.13	0.89	1.45	0.319	1.14	0.88	1.47	0.317
Time of diagnosis								
2000–2008	1.00				1.00			
2009–2016	0.68	0.60	0.78	<0.001	0.68	0.58	0.80	<0.001
Catchment area								
Helsinki	1.00				1.00			
Turku	1.46	1.19	1.81	0.001	1.53	1.23	1.90	<0.001
Tampere	1.33	1.09	1.63	0.005	1.35	1.09	1.67	0.006
Kuopio	1.58	1.31	1.90	<0.001	1.53	1.24	1.88	<0.001
Oulu	1.37	1.09	1.73	0.007	1.39	1.10	1.77	0.007
Surgery								
PD	1.00				1.00			
DPR	0.72	0.58	0.90	0.004	0.79	0.63	0.99	0.039
TP	1.22	0.92	1.63	0.169	1.35	1.01	1.82	0.043
Other	1.03	0.62	1.73	0.897	0.98	0.59	1.66	0.951
Oncological treatment								
None	1.00				1.00			
Only neoadjuvant	0.96	0.59	1.56	0.866	1.21	0.74	1.98	0.458
Only adjuvant	0.60	0.46	0.78	<0.001	0.74	0.56	0.97	0.027
Time dependent*	1.02	1.01	1.02	0.002	1.02	1.01	1.03	0.001
Perioperative	0.34	0.20	0.57	<0.001	0.52	0.30	0.89	0.016
Time dependent*	1.03	1.01	1.04	0.001	1.03	1.01	1.04	0.001

HR = Hazard ratio, CI = confidence interval, CCI = Charlson Comorbidity Index, PD = Pancreaticoduodenectomy, DPR = Distal pancreatic resection, TP = Total pancreatectomy.
* Time dependent correction term per month.

oncological treatments were especially low in the early 2000s. Comparing the oncological data of the local register of Helsinki University Central Hospital area and HILMO registry, we found a partial incompleteness of the oncological data in the HILMO register. However, across all treatment groups, survival associated with oncological therapy data, whilst treatment group proportions compared favourable to existing literature. In the multivariate analysis, adjuvant therapy that was started more than 6 months after the radical operation was deemed palliative. We acknowledge that this might include some patients who had a recurrent disease diagnosed already, but it's impossible to distinguish definitely curative-intent and palliative oncological treatment from the data. Some patients did not have histological confirmation so false diagnoses might be included. Disease stage corresponding to the Union for International Cancer Control TNM Classification of Malignant Tumors was not available from the Finnish Cancer Register data. Concomitant vascular procedures could not be identified because of lack of systematic coding. Follow-up data were available from Statistics Finland until the end of 2018 and, thus, some patients had a shorter follow-up period.

5. Conclusions

In Finland, survival amongst pancreatic cancer patients, particularly those who underwent radical surgery, improved during the 2000 to 2016. Although the proportion of patients undergoing diagnostic surgery decreased, we found no increase in the radical intent resection rate. Thus, the improvement in survival is likely due to the advancements in the oncological treatments. Prognosis associated with metastasised disease remains poor.

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CRediT authorship contribution statement

Panu Aaltonen: Data curation, Formal analysis, Writing – original draft. **Olli Carpén:** Conceptualization, Writing – review & editing. **Harri Mustonen:** Formal analysis, Writing – review & editing. **Pauli Puolakkainen:** Supervision, Writing – review & editing. **Caj Haglund:** Conceptualization, Writing – review & editing. **Katriina Peltola:** Resources, Writing – review & editing. **Hanna Seppänen:** Supervision, Project administration, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at

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