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National compliance to an evidence-based multidisciplinary guideline on pancreatic and periampullary carcinoma

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ABSTRACT

Background: We evaluated national compliance to selected quality indicators from the Dutch multidisciplinary evidence-based guideline on pancreatic and periampullary carcinoma and identified areas for improvement.

Methods: Compliance to 3 selected quality indicators from the guideline was evaluated before and after implementation of the guideline in 2011: 1) adjuvant chemotherapy after tumor resection for pancreatic carcinoma, 2) discussion of the patient within a multidisciplinary team (MDT) meeting and 3) a maximum 3-week interval between final MDT meeting and start of treatment.

Results: In total 5086 patients with pancreatic or periampullary carcinoma were included. In 2010, 2522 patients were included and in 2012, 2564 patients. 1) Use of adjuvant chemotherapy following resection for pancreatic carcinoma increased significantly from 45% (120 out of 268) in 2010 to 54% (182 out of 336) in 2012 which was mainly caused by an increase in patients aged <75 years. 2) In 2012, 64% (896 of 1396) of patients suspected of a pancreatic or periampullary carcinoma was discussed within a MDT meeting which was higher in patients aged <75 years and patients starting treatment with curative intent. 3) In 2012, the recommended 3 weeks between final MDT meeting and start of treatment was met in 39% (141 of 363) of patients which was not influenced by patient and tumor characteristics.

Conclusion: Compliance to three selected quality indicators in pancreatic cancer care was low in 2012. Areas for improvement were identified. Future compliance will be investigated through structured audit and feedback from the Dutch Pancreatic Cancer Audit.

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Introduction

Pancreatic cancer is a devastating disease affecting approximately 10–12 per 100,000 persons per year [1–3]. Only around one in every five patients presents with resectable disease, surgical resection

being the only curative treatment option [4,5]. Palliative treatment offers a limited survival benefit and some improvement in quality-of-life [6]. Total 5-year survival rates are as low as 3–6% [1,7,8].

Both national and international developments regarding diagnostic strategies and treatment options, and the participation of various medical disciplines mandate uniform evidence-based guidelines on pancreatic and periampullary cancer. Quality indicators in pancreatic cancer care are scarce and mainly focus on pancreatectomy case volume [9]. However, guideline compliance in the management of pancreatic cancer has been associated with

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improved survival [10]. The Dutch National Working Group on Gastrointestinal Tumors (LWGIT) therefore developed a multidisciplinary evidence-based guideline which was guided and financed by the Dutch Comprehensive Cancer Center [11]. The guideline was implemented in The Netherlands in 2011 and comprises both pancreatic and periampullary carcinomas [12].

The aim of this study was to evaluate national compliance to 3 selected quality indicators from the guideline and to identify areas for improvement of compliance. The 3 quality indicators were selected based on their relevance and potential benefit. Selected quality indicators were the use of adjuvant chemotherapy following tumor resection for pancreatic carcinoma, the discussion of a patient with a suspected pancreatic or periampullary carcinoma within a multidisciplinary team (MDT) meeting, and a maximum transit time of 3 weeks between final MDT meeting and the start of potentially curative treatment.

Methods

Patient selection

Patients diagnosed with an invasive pancreatic or periampullary carcinoma in The Netherlands between 2010 and 2012 were selected from the database of the Dutch National Cancer Registry (NCR), which covers nearly 17 million inhabitants. Patients diagnosed at autopsy, <18 years old at diagnosis, with a non-invasive tumor or diagnosed abroad were excluded. Patients receiving surgery abroad were excluded from the analyses of compliance to the selected indicators.

Data acquisition

Specially trained registration-employees of the NCR gather data on patient (age, sex), tumor (date of diagnosis, morphology, topography, stage) and treatment (tumor resection, surgical exploration, chemotherapy) characteristics from medical files in all Dutch hospitals. Data were not regularly available on the occurrence of MDT meetings and on time intervals between MDT meetings and the start of treatment. These were therefore additionally collected for patients diagnosed between May 1st and December 31st of 2012.

Conforming to guideline recommendations, the use of adjuvant chemotherapy was evaluated only for patients with a pancreatic carcinoma. Discussion of a patient within a MDT meeting was evaluated for all patients diagnosed with a pancreatic or periampullary carcinoma. Only patients who started potentially curative treatment for pancreatic or periampullary carcinoma were selected in the evaluation of the time interval between the final MDT meeting and the start of (neoadjuvant) treatment.

Hospitals were divided into academic, top-clinical and general hospitals (in 2012 respectively 8, 28 and 57 hospitals). Hospital volume was calculated based on respectively the true number of resections and the number of planned resections. Regions were divided based on (previous) NCR regions. For one region in The Netherlands no data on the occurrence or dates of a MDT was available.

Statistical analysis

Data were analyzed using STATA/SE (version 13.0; STATA Corp., College Station, Texas, USA). Populations were compared using chi-square tests. Case-mix corrected data were compared using likelihood ratio test. Differences between hospitals and regions were corrected for sex, age (<60, 60–74, 75+), tumor location and TNM-stage. Results were considered statistically significant at a p-value below 0.05. For the analysis of variation between hospitals patients

who initiated tumor-directed treatment (resection or chemo(radio)therapy) were classified based on the hospital of treatment and the remainder of patients were classified based on the hospital of clinical diagnosis.

Results

In total 5086 patients with a pancreatic or periampullary carcinoma were included. In 2010, in total 2522 patients were included of which 2159 (86%) patients had a pancreatic carcinoma. Of these patients, 685 (27%) patients underwent surgical exploration. In 2012, 2564 patients with a pancreatic or periampullary (of which 83% with pancreatic carcinoma) were included, of which 765 (30%) patients underwent surgical exploration. [Table 1](#) depicts patient and tumor characteristics. Neoadjuvant therapy was only administered sporadically during the study period (1.6% of all patients with pancreatic carcinoma that underwent surgical exploration in 2012).

First indicator: use of adjuvant chemotherapy

The use of adjuvant chemotherapy following resection of a pancreatic carcinoma increased significantly from 44% (121 of 275 patients) in 2010 to 54% (182 of 336 patients) in 2012 ($p = 0.02$, [Table 2](#)). This was mainly caused by an increase in patients aged younger than 75 years, where the use of adjuvant chemotherapy increased from 51% to 63% ($p = 0.008$). In patients aged 75 years or older there was a non-significant increase (10%–16%). In 2010, in hospitals with lower resection volumes fewer patients received adjuvant chemotherapy compared to hospitals with higher resection volumes (28–52%, $p = 0.02$). In 2012 these differences were non-significant (25–59%, $p = 0.13$). In 2010 and 2012 there were no significant differences between academic, top-clinical or general hospitals.

Second indicator: discussion of a patient within a MDT meeting

Of all patients diagnosed with pancreatic or periampullary carcinoma in 2012, 64% (896 of 1396 patients) had been discussed within a MDT meeting ([Table 3](#)). Patients aged 75 years and older were significantly less often discussed (51%) within a MDT meeting compared to patients younger than 75 years (72%, $p < 0.001$).

Of all patients who initiated tumor-directed treatment, 22% had not been discussed within a MDT. In patients who underwent surgical exploration this percentage was lower (15%) compared to patients receiving palliative chemo(radio)therapy (33%, $p < 0.001$). Of patients not receiving treatment, 50% had not been discussed within a MDT.

Both patients receiving tumor-directed treatment and patients not receiving tumor-directed treatment were less often discussed within a MDT in a general hospital compared to patients in an academic or top-clinical hospital ($p < 0.001$ for both groups).

Third indicator: time interval between final MDT meeting and start of treatment

Of all patients receiving potentially curative surgery in 2012, 39% (141 of 363 patients) underwent surgical exploration or started neoadjuvant treatment within 3 weeks following the final MDT meeting. Patient and tumor characteristics did not influence this result ([Table 4](#)).

In academic hospitals fewer patients (33%) started potentially curative treatment within 3 weeks following the final MDT meeting compared to top-clinical (47%) and general hospitals (45%, $p = 0.02$).

Table 1

Patient and tumor characteristics of patients diagnosed in 2010 and 2012 with a pancreatic or periampullary carcinoma, or only a pancreatic carcinoma, respectively.

2010–2012	Pancreatic- and periampullary carcinoma			Pancreatic carcinoma		
	2010	2012	Chi ²	2010	2012	Chi ²
	N = 2522 (%)	N = 2564 (%)	p-Value	N = 2159 (%)	N = 2122 (%)	p-Value
Sex			0.77			0.80
Male	1276 (51)	1308 (51)		1074 (50)	1064 (50)	
Female	1246 (49)	1256 (49)		1085 (50)	1058 (50)	
Age			0.44			0.47
<60 years	431 (17)	431 (17)		374 (18)	354 (17)	
60–74 years	1142 (45)	1206 (47)		988 (46)	1011 (48)	
≥75 years	949 (38)	927 (36)		797 (37)	757 (36)	
Stage ^a			n.a.			n.a.
TNM – I (T1-2N0M0)	136 (5)	236 (9)		75 (3)	168 (8)	
TNM – II (T3N0M0, T1-2-3N1M0)	425 (17)	606 (24)		319 (15)	459 (22)	
TNM – III (T4M0)	214 (9)	312 (12)		179 (8)	265 (13)	
TNM – IV (M1)	887 (35)	1260 (49)		804 (37)	1154 (54)	
TNM – X	82 (3)	115 (5)		35 (2)	47 (2)	
No TNM-info (diagnosis 2010)	779 (31)	35 (1)		747 (35)	29 (1)	
Hospital of first visit			<0.001			0.001
Academic	311 (12)	238 (9)		256 (12)	195 (9)	
Top-clinical	1171 (46)	1137 (44)		1007 (47)	943(44)	
General	1040 (41)	1189 (46)		896 (42)	984(46)	
Hospital of pathological diagnosis ^b			0.05			0.01
Academic	450 (18)	523 (20)		361 (17)	426 (20)	
Top-clinical	1199 (48)	1159 (45)		1033 (48)	955 (45)	
General	873 (35)	882 (34)		765 (35)	741 (35)	
Treatment ^c			0.01			0.02
Surgical exploration	685 (27)	765 (30)		483 (22)	506 (24)	
Other tumor-directed treatments	405 (16)	450 (18)		379 (18)	426 (20)	
No tumor-directed treatment	1432 (57)	1349 (53)		1297 (60)	1190 (56)	

^a Based on pTNM supplemented with cTNM. NX and MX were classified as N0 and M0.^b When no pathological diagnosis was available, hospital of clinical diagnosis was selected.^c Other tumor-directed treatments: chemo(radio)therapy not followed by surgery, radiotherapy for metastases and sporadically radio frequent ablation (RFA) or irreversible electroporation (IRE). No tumor-directed treatment: no treatment or symptom-relief only.

Discussion

National compliance to 3 selected quality indicators from the Dutch evidence-based guideline on pancreatic carcinoma was low in 2012. Following resection of a pancreatic carcinoma, patients in adequate clinical condition should receive adjuvant chemotherapy [13,14]. However, in total only 54% of patients received adjuvant chemotherapy in 2012. Use of adjuvant chemotherapy significantly increased following implementation of the guideline in 2011 which was mainly caused by an increase in patients younger than 75 years old. Possibly, adjuvant chemotherapy is precluded in older patients due to a consequently worse performance status or increased

comorbidity compared to younger patients, however we had no data available on this issue. With the exception of a hospital volume category of less than 10 resections per year, the number of patients receiving adjuvant chemotherapy increased in each higher hospital volume category. Possibly low volume hospitals are less aware of guideline recommendations. Many studies have already demonstrated improved postoperative and long-term survival following pancreatic surgery in hospitals with higher procedural volumes as compared to low volume hospitals [15–18]. Over the past decade, centralization of pancreatic surgery has also been observed in The Netherlands which was accompanied by a decrease in post-operative mortality [19–21].

Table 2

Use of adjuvant chemotherapy following resection of pancreatic carcinoma.

	2010		2012		Increase?
	Numerator/denominator ^b	Indicator value	Numerator/denominator	Indicator value	Chi ² p-value
All patients	120/268	45%	182/329	54%	0.02
Age		***p < 0.001		***p < 0.001	
<60 years	43/64	67%	48/67	72%	0.58
60–74 years	73/162	45%	123/204	60%	0.004
≥75 years	4/42	10%	9/58	16%	0.38
Stage ^a		p = 0.43		***p < 0.001	
TNM – I (T1-2N0M0)	16/46	35%	10/42	24%	0.26
TNM – II (T3N0M0, T1-2-3N1M0)	95/203	47%	163/276	59%	0.008
TNM – III (T4M0)	7/16	44%	7/11	64%	0.31
TNM – X	2/3	67%	–	–	n.a.
Radicality of resection		p=0.15		p=0.77	
R0	90/188	48%	118/217	54%	0.19
R1-2	28/70	40%	56/103	54%	0.06
RX	2/10	20%	6/9	67%	0.04

^a Based on pTNM. NX and MX were classified as N0 and M0.^b All patients that received resection of pancreatic (adeno)carcinoma.

Table 3
Frequency of discussion of patients with pancreatic or periampullary carcinoma within multidisciplinary team meeting.

	Tumor-directed treatment (2012)			No tumor-directed treatment (2012)		
	Numerator/denominator ^c	Indicator value	p-Value	Numerator/denominator ^d	Indicator value	p-Value
All patients ^a	543/694	78%		353/702	50%	
Treatment			<0.001			
Curative intent	375/442	85%				
Other tumor-directed treatments	168/252	67%				
No tumor-directed treatment				353/702	50%	
Age			0.44			<0.001
< 60 years	123/163	75%		44/70	63%	
60–74 years	326/408	80%		149/255	58%	
≥75 years	94/123	76%		169/337	42%	
Tumor location			0.05			0.86
Pancreas	412/538	7%		311/617	50%	
Periampullary	131/156	84%		43/85	49%	
Stage ^b			<0.001			<0.001
TNM – I (T1-2N0M0)	40/53	75%		38/73	52%	
TNM – II (T3N0M0, T1-2-3N1M0)	237/270	88%		52/82	63%	
TNM – III (T4M0)	81/97	84%		51/65	78%	
TNM – IV (M1)	181/270	67%		192/424	45%	
TNM – X	4/4	100%		20/58	34%	

^a Excluding 86 patients in which information on dates was absent (6% of selection period and regions).

^b Based on pTNM, supplemented with cTNM. NX and MX were classified as N0 and M0.

^c All patients suspected of a pancreatic or periampullary carcinoma that received tumor-directed treatment (i.e. surgical exploration or chemo(radio)therapy).

^d All patients suspected of a pancreatic or periampullary carcinoma, that did not receive tumor-directed therapy.

Due to an increasing number of available treatment options, MDT meetings are considered essential for each patient and not only to discuss possible surgical treatment. In 2012 this was not yet evident in The Netherlands. As the survival of older patients is similar to younger patients following surgery, age should not preclude surgery [22]. However, patients older than 75 years were less often discussed in a MDT compared to patients younger than 75 years old. Possibly it is anticipated that there is a worse preoperative condition of the patient to be eligible for surgery, however these aspects should be weighed during the MDT meeting itself. Indeed, perhaps older patients should even be more often discussed within a MDT meeting because of co-morbid diseases and relatively poor performance status. Possibly, some elderly patients may have refused to undergo high-risk pancreatic surgery. Patients

that underwent surgical exploration were more often discussed within a MDT compared to patients who did not. Possibly more patients would be eligible for curative treatment if they had been discussed within a MDT. However, in multiple hospitals MDT meetings seem to be selectively utilized.

Due to the participation of patient organizations in the development of the guideline there has been an increased attention for shorter transit times. A maximum time interval of three weeks between the final MDT meeting and the start of potentially curative treatment was chosen by the guideline committee as this was considered feasible for all hospitals to perform additional diagnostics if necessary, and to plan the operation. Various factors such as a patient's preoperative condition and the need for preoperative biliary drainage may slow transit times. Preoperative

Table 4
Percentage of patients with maximum transit time of 3 weeks between final MDT meeting and the start of potentially curative treatment.

	Start treatment with curative intent (2012)				
	Numerator/denominator ^c	Indicator value	p-Value	Mean (SD), in days	Median (p25–p75), in days
All patients	141/363	39%		30 (21)	28(15–39)
Treatment ^a			0.97		
Resection	107/270	39%		30(21)	28(15–39)
Surgical bypass	22/56	39%		33(21)	28(14–39)
Exploration only ('open-close')	11/32	34%		28(15)	26,5(13,5–37)
Neoadjuvant treatment	1/5	20%		38(19)	41(26–46)
Age			0.10		
<60 years	31/6	47%		24(14)	25(12–32)
60–74 years	89/228	39%		30(22)	28(15–39)
≥75 years	21/72	29%		34(20)	32,5(20–42)
Tumor location			0.76		
Pancreas	95/250	38%		32(14)	31(24–37)
Periampullary	46/116	40%		30(21)	28(14–39)
Stage ^b			0.93		
TNM – I (T1-2N0M0)	12/37	32%		35(29)	28(19–42)
TNM – II (T3N0M0, T1-2-3N1M0)	88/222	40%		30(20)	28(15–39)
TNM – III (T4M0)	19/47	40%		26(17)	26(13–35)
TNM – IV (M1)	21/57	37%		28(19)	27(14–39)
TNM – X	1/3	33%		46(45)	23(17–97)

^a Excluding patients where date of start of treatment was not available.

^b Based on pTNM, supplemented with cTNM. NX and MX classified as N0 and M0.

^c All patients with a malignant pancreatic or periampullary tumor that underwent surgical exploration following multidisciplinary team meeting.

biliary drainage may increase the rate of postoperative complications, as was demonstrated in patients undergoing surgery for pancreatic head cancer [23]. However, the maximum time interval of 3 weeks following MDT meeting to surgery or neoadjuvant treatment is an important quality indicator and was most often achieved in top-clinical and general hospitals. Improved hospital logistics, collaborations or tumor-specific MDT's may increase compliance to this quality indicator.

It was challenging in which hospital a MDT meeting should be registered. Many patients start a diagnostic pathway in hospital A but are consequently referred to hospital B where pathological diagnosis, MDT meeting and possibly treatment are performed. Registering the MDT meeting in hospital B probably fails many referring hospitals. However, registering the MDT meeting in hospital A - as the hospital responsible for adequate referral of potentially curable patients - does not reflect the true situation. We therefore chose a partition. For the analysis of variation between hospitals, patients who initiated tumor-directed treatment (resection or chemo(radio)therapy) were classified based on the hospital of treatment and the remainder of patients were classified based on the hospital of clinical diagnosis. With the exception of a few general hospitals, data on MDT meetings was available in all (digital) medical files used by registration employees. Therefore only a slight under-registration in general hospitals on the number of patients discussed within MDT meetings is possible.

In order to stimulate and monitor further compliance to the guideline, continuous audit and feedback at a hospital level is recommended, with attention to 'best practices'. Examples include the recently started audit systems in the Netherlands by the Dutch Institute for Clinical Auditing (DICA), which also include an audit for pancreatic carcinoma [24]. In the Dutch Pancreatic Cancer Audit (DPCA) patient-, tumor- and surgical characteristics are registered, as are the treatment results of patients receiving a pancreatic resection [25]. In future these data will be shared with both health care providers and patients, so that transparency may contribute to improvement in the quality of care with adequate case-mix correction. Furthermore, the Dutch Comprehensive Cancer Center reports periodically to all hospitals on all patients diagnosed with a pancreatic or periampullary carcinoma.

Based on a nationwide evaluation, compliance to a multidisciplinary evidence-based guideline on pancreatic and periampullary carcinoma was low. A significantly increased amount of patients should receive adjuvant chemotherapy. Non-compliance to this quality indicator seems to be mainly affected by older age. Although a slight improvement was seen before and after implementation of the guideline, a longer study period is needed to evaluate compliance changes. The percentage of patients discussed within a MDT should approach 100% and non-compliance seems to be affected by a patient's older age and not starting treatment with curative intent. A significantly increased amount of patients should experience faster transit times between the final MDT meeting and start of treatment. Better hospital logistics, collaborations or tumor-specific MDT's between regions may here contribute to improvement.

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