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Are survival predictions reliable? Hospital volume versus standardisation of histopathologic reporting for accuracy of survival estimates after pancreatoduodenectomy for adenocarcinoma

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ABSTRACT

Histopathologic reporting after pancreatoduodenectomy is often non-standardised. Inappropriate reporting may bias survival estimates and make comparison between institutions difficult. Using population-based nationwide data from the Cancer Registry of Norway, we examined the influence on survival estimates of standardised histopathologic reporting versus non-standardised histopathologic reporting after pancreatoduodenectomy for adenocarcinomas in the pancreas, distal bile duct, ampulla and duodenum ($n = 506$). Standardised histopathologic reports from a study hospital ($n = 113$) were compared with reports from all other institutions (24 hospitals; $n = 393$) discriminating between high/medium-volume and low-volume institutions. In the study hospital, more tissue blocks were sampled, more nodes were evaluated, and more details about resection margins, size, origin and vascular and perineural infiltration were reported ($p < 0.001$). Multivariable survival analysis identified lymph node involvement as the factor that is most dependent on standardised reporting to discriminate between favourable and poor prognostic subgroups ($p = 0.018$). Standardised evaluation was more important than hospital volume for completeness of histopathologic reporting and for accuracy of survival estimates.

1. Introduction

Adenocarcinomas in the pancreatic head are most often non-resectable, and even when curative-intent resection is performed, most patients die within a few years.[1,2] Adjuvant treatment trials on advanced and resected pancreatic cancer have shown only limited effect,[3] and new treatment options are urgently needed.[4] In order to translate laboratory research findings into clinical practice, the first step should be to ascertain that information on histopathologic prognostic factors is available for every resected patient, and is recorded in a way that facilitates comparability between groups of patients.

In spite of many efforts to standardise assessment of pancreatoduodenectomy specimens,[5–15] histopathologic report-

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ing after pancreatic head resections is frequently non-standardised,[13–15] even in multicentre studies.[16] Non-standardised reporting could lead to underestimation of the presence of poor prognostic factors such as resection margin involvement[13] and regional lymph node metastasis,[17] due to lack of systematic investigation of the resected specimen. Failure to recognise resection margin or lymph node involvement would in turn negatively skew survival estimates for allegedly margin-free or node-free resected patients. Moreover, the precise tumour origin of adenocarcinomas resected by pancreatoduodenectomy (pancreatic, ampullary, distal bile duct or periampullary duodenal) may be difficult to determine.[7,14,18–23] Inclusion of prognostically more favourable, non-pancreatic tumours in reports of pancreatic head resections could thus skew survival estimates in a positive direction.[24,25] Standardisation of histopathologic evaluation should be an effective measure to increase the quality of histopathologic reporting, and also ensures adequate inclusion and stratification for clinical trials.

The direct impact on accuracy of survival estimates derived from standardised histopathologic reporting versus non-standardised histopathologic reporting of solid cancers to our knowledge has not been evaluated previously, using population-based nationwide data comparing the independent importance of each factor reported. The aim of this study was to evaluate whether standardised histopathologic reporting after curative-intent pancreatoduodenectomy for adenocarcinoma improves the registration of the prognostic factors tumour size, lymph node involvement, resection margin involvement, and tumour origin (pancreatic, ampullary, distal bile duct or duodenal), adjusting for importance of surgical volume. Furthermore, we wanted to assess the consequences for survival estimates based on these factors comparing standardised reporting versus non-standardised reporting.

2. Patients and methods

2.1. Patients

The Cancer Registry of Norway receives mandatory reports on all cases of cancer diagnosed or treated in Norway (population 4.6 million in 2004).[26,27] By law and according to the Cancer Registry Regulations, data on verified and suspected cancers are collected from all hospitals and pathology institutions and are made available for researchers as deidentified files. From the Cancer Registry, 506 patients who underwent curative-intent pancreatoduodenectomy for pancreatic head adenocarcinoma in Norway from 1998 to 2004, inclusive, were identified. For each patient, the following information was electronically retrieved from the Cancer Registry: age, gender, date of surgery and the anatomic site of cancer origin. One patient was diagnosed with two separate adenocarcinomas in the pancreatic head, originating from the ampulla and the pancreas, respectively. For the purpose of the current study, this patient was classified as having a single tumour originating from the pancreas.

Among the 506 pancreatoduodenectomies for adenocarcinomas, 113 were performed at the study hospital, a third-level referral hospital with standardised histopathologic assessment and reporting of pancreatoduodenectomy specimens.[14] Basis for standardised reporting at this hospital included the use of a standardised protocol for gross examination, specimen dissection, tissue sampling and microscopic assessment. The template that is currently used for summarising the most important histopathologic findings

DIAGNOSIS
PANCREATODUODENECTOMY SPECIMEN WITH
WELL / MODERATELY / POORLY / ANAPLASTIC DIFFERENTIATED ADENOCARCINOMA OF
PANCREATOBILIARY / INTESTINAL / _____ (other) HISTOLOGIC TYPE
ORIGINATING FROM THE **PANCREAS / DISTAL BILE DUCT / AMPULLA VATERI / DUODENUM**
WITH INFILTRATION INTO THE **PANCREAS / DISTAL BILE DUCT / AMPULLA VATERI / DUODENUM**

Extent of tumour growth
Tumour size (largest diameter): **____mm**
Resection margin, distal bile duct: **free by minimum ____ mm / involved**
Resection margin, pancreatic neck: **free by minimum ____ mm / involved**
Resection margin, retroperitoneal (posterior): **free by minimum ____ mm / involved**
Involvement of large vessels: ____ (Resection margin: **free by minimum ____ mm / involved**)
Infiltration to anterior (serosal) margin: **detected / not detected**
Infiltrasjon to stomach: **detected / not detected**

Nodal involvement
Regional lymph nodes: **____ positive**. Total number of regional nodes evaluated: ____
Other lymph nodes: **____ positive** in _____ (location). Total number of other nodes evaluated: ____

Other histopathologic characteristics
Small-vessel involvement: **detected / not detected;** in **blood / lymph** vessels
Perineural involvement: **detected / not detected**
PanIN, **grade ____ detected / not detected** (in pancreatic ducts)
BilIN, **grade ____ detected / not detected** (in biliary ducts)

pTNM (dependent on tumour origin): ____

Additional pathology

Fig. 1 – Template for standardised histopathologic reporting of pancreatic head adenocarcinoma specimens that is currently used at Rikshospitalet University Hospital (study hospital). In addition to the diagnosis and conclusion reported using this template, the histopathologic reports consist of a gross description that may include macroscopic photos, and a specific report on the microscopic examination for each block.