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An international survey-based study on colorectal cancer pathology reporting – guidelines versus local practice.

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Abstract:

Aims

Different guidelines for colorectal cancer (CRC) pathology reporting have been published. We aimed to identify differences between publicly available CRC reporting guidelines and to survey pathologists from different countries to establish the degree of guideline implementation in local routine practice.

Methods and results

We compared all core and non-core items of CRC reporting guidelines to identify discrepancies. We then created a survey, which was sent out to 782 pathologists practicing in 30 different countries. It included questions on the demographics of the reporting pathologist as well as resection specimen handling and microscopic evaluation, grading, staging and additional techniques, such as immunohistochemistry or molecular pathology.

First, core and non-core items of five national CRC reporting guidelines were compared and 12 items were found to differ. Different items are considered core or non-core by different guidelines and more than one TNM staging edition was applied across guidelines. The survey was completed by 143 pathologists from 30 countries. We identified differences between local practice and guidelines with potential clinical impact, e.g. tumour budding was never reported by 28.7% of responders, although it has prognostic value for survival in stage II CRC.

Conclusions

This is the first international study comparing CRC pathology reporting guidelines with real world local practices. There are differences in CRC pathology reporting guidelines and in guideline implementation into local practice, both with potential impact on patient care. Harmonization of datasets, use of templates and audits of local pathology practice are needed to ensure best possible quality of CRC pathology reporting.

Keywords:

Colorectal cancer, guidelines, Pathology reporting, international survey

Word count: 3462

Introduction

Colorectal cancer (CRC) is the third most common diagnosed cancer and the fourth most common cause of cancer death in the world, with 1.4 million new cases and 694,000 deaths in 2012 [1]. Standardized diagnostic pathology procedures are a key factor for appropriate treatment of CRC patients [2].

CRC pathology reporting guidelines have been published in several countries to ensure that all clinically relevant information is included in the pathology report. They usually include so called 'core' and 'non-core' elements. Core items are required for cancer staging, patient management and prognosis and are supported by strong evidence, e.g. resection margin status [3]. Non-core elements should ideally be included in the report to meet clinical or research needs at the local level, e.g. tumour budding (TB)[3]. Interestingly, the same item (for example perineural invasion (PNI)) is considered core in one national dataset and non-core in the dataset of another country [3-4]. which can lead to problems when comparing data especially in the setting of an international clinical trial or cancer registries.

A number of CRC pathology reporting audits have been conducted in the past. Most of them were performed at either local [5-9], regional [10-17] or national level [18-19] and assessed the adherence to national pathology guidelines by reviewing pathology reports.

The aim of our study was to (a) compare CRC pathology reporting guidelines from different countries and (b) to assess how local pathologists implement existing guidelines.

Materials and methods

Comparing national CRC reporting guidelines

Prior to creating the survey, the authors reviewed CRC reporting guidelines from the Royal College of Pathologists, London (UK) (RCPath) (3rd edition, 2014) [3], the Royal College of Pathologists of Australasia (RCPA) (3rd edition, 2016)[20], the College of American Pathologists (CAP) (7th edition, 2016)[4] , the Spanish Society of Pathology (SEAP) "Libro blanco 2017" (5th edition, 2017) [21] and the Italian group of Digestive Pathology and Italian Society of Pathology and Diagnostic Cytology – Italian division of International Academy of Pathology (GIPAD/ SIAPEC-IAP) guidelines (2011) [22]. These guidelines were chosen because they represented major pathology organisations and because they were the most updated versions at the time when survey was sent out. By the time of the publication, RCPath dataset and CAP protocol have been updated in October 2017 and June 2017 respectively [23-24].

We included core as well as non-core items. For each item, we recorded if it was core or non-core in the guideline we reviewed. Moreover, we recorded the differences in wording or values encountered in our search.

Designing the survey

The following items were included in the survey: demographic data of the reporting pathologist, CRC resection specimen handling, microscopic evaluation of the resection specimens, grading and staging system used, use of additional techniques such as immunohistochemistry or molecular pathology, and name of the guideline(s) used by the responder. The choice of these items was based on the identified differences between different national datasets. In total, the survey contained 35 questions concerning CRC pathology reporting, of which 23 questions focused on local practice, 8 questions on the characteristics of the survey participant and their institution and 4 questions on the implementation of CRC pathology guidelines or templates for reporting. The full questionnaire can be found in the electronic supplementary material. The survey was designed by three pathologists with special interest in gastrointestinal (GI) pathology (M.U., H.G. and J-F.F.). A pilot version was tested by an independent team of three general pathologists. The revised and final questionnaire was emailed to 782 recipients from academic institutions, general hospitals, cancer centers and private practice in 33 different countries in June 2017. Our network included pathologists involved in the European Organization for Research and Treatment of Cancer (EORTC), European Society of Pathology (ESP) Gastrointestinal Working Group and other organizations, such as European Network of Gastrointestinal Pathology among others.

Descriptive statistical analysis was performed. We used proportions for qualitative variables. The analyses were conducted using SAS 9.4 (SAS, Cary, NC).

Results

Comparison of core and non-core items of five national CRC reporting guidelines

Currently, the CRC pathology reporting guidelines differ on a national [3,20,4,21-22] as well as local level (data from a survey responder) with respect to what is recognized as mandatory (core) or optional (non-core) item.

For example, regarding microscopic evaluation, RCPath [3] includes venous invasion as core data and lymphatic invasion as non-core data, which is similar to GIPAD/SIAPEC-IAP guidelines [22]. The latter, however, require only a statement about the presence or absence of extramural venous invasion. CAP considers distinction between venous and lymphovascular invasion (LVI) as optional, while RCPA and SEAP consider it as core item and require

distinction between intra- or extramural. Interestingly, PNI is a core data item only in the CAP protocol, while SEAP doesn't cover this item at all. The other guidelines include it as a non-core item [3,20,4,21-22].

There are minor differences between the guidelines with respect to the assessment of tumour regression grade after chemo(radio)therapy. All of the reviewed datasets, except GIPAD/SIAPEC-IAP, present a 4-tiered system based on a modified Ryan Scheme [25]. However, each guideline uses a slightly different wording. GIPAD/SIAPEC-IAP includes a 3-tiered scheme based on the RCPath guidelines [3,20,4,21-22].

Other important differences between the datasets include recommendations on which TNM staging edition should be used. RCPA, CAP, SEAP, and GIPAD/SIAPEC-IAP protocols were based on the AJCC or AJCC/UICC 7th edition of TNM [26], while RCPath dataset was based on the UICC 5th edition of TNM [27]. The Dutch CRC reporting guideline also recommended use of TNM 5th [28]. The use of different TNM staging systems can potentially lead to over- or understaging of the same specimen which can impact treatment decisions or eligibility criteria for entry into a clinical trial. However, the updated versions of RCPath dataset and CAP protocols refer to the 8th TNM edition [23-24].

Furthermore, there are items included in some but not all of the guidelines. One example is the maximum distance of tumour spread beyond the muscularis propria in mm, which is a core data item in RCPath dataset [3], while it is recommended in RCPA guidelines as an alternative to TNM [20] and not mentioned at all in the CAP protocol [4], SEAP guidelines [21], or in GIPAD/SIAPEC-IAP guidelines [22]. Details on items that differ between guidelines can be found in Table 1.

Characteristics of the responders

A total of 143 responses (response rate 18.3%) were received from 30 countries, 138 (96.5%) of which were from Europe and 5 (3.5%) from non-European countries (Fig.1). The database was cleaned by deleting double data entries. There were 95 (66.4%) of responders who declared working in academic institutions, 35 (24.5%) in general hospitals, 19 (13.3%) in cancer centers and 14 (9.8%) in private practice. 77 (53.8%) responders were pathologists with a special interest in GI pathology and 66 (46.2%) responders were general pathologists. The characteristics of the pathologists are presented in Table 2 and Fig.2.

As the survey items were not obligatory, 28 of 35 questions were only answered by some of the responders amounting to missing responses from 2 to 9 responders per question (missing data 1.4% - 6.3%). 135 (94.4%) responders answered at least 30 questions. The percentages presented in the results are proportions of all respondents (n=143 being 100%), unless stated otherwise. Although the majority of the responders were European (n=138), we took into account also the

responders from non-European countries, to get a broader overview of pathology reporting guidelines used worldwide.

CRC resection specimen handling

58 (40.6%) departments receive colon and rectum resections fresh, 10 (7.0%) receive only rectum resections fresh and 71 (49.7%) of the responders receive colon and rectum resections fixed. For further details on specimen handling per responder see Table 3.

Microscopic evaluation of CRC specimens

LVI was always reported by 131 responders (91.6%), while 10 (7.0%) responders reported it only when positive. The level of the deepest venous spread was reported by 82 (57.3%) and omitted by 52 (36.4%) responders. PNI was always reported by 103 (72%) responders, while 32 (22.4%) responders reported it only when positive, and 6 (4.2%) responders never reported it. TB was always reported by 52 (36.4%) responders, while 48 (33.6%) responders reported it only in selected cases and 41 (28.7%) responders never reported it. For details see Table 3.

Grading and staging system used for CRC specimens

Regarding staging system, the most commonly applied was the 8th edition of TNM which was used by 55 responders (38.5%), followed by the 7th edition (n=50, 35.0%), the 5th edition (n=34, 23.8%), and the 6th edition (n=1, 0.7%). The use of the 5th edition of TNM is related to responders from the UK (n=28) and the Netherlands (n=6), as RCPath guidelines (3rd edition) and Dutch guidelines were based on this edition at the time of the survey. Interestingly, 17.8% (n=5) of the UK-based responders nevertheless used either TNM 7th or 8th edition. While the majority of the pathologists used only TNM for staging, 42 (29.4%) responders also used other systems, such as the Dukes or Astler Coller staging systems. For details see Table 3.

Use of additional techniques (IHC, molecular pathology)

43 (30.1%) responders performed microsatellite instability testing for every case, while 91 (63.6%) responders performed it in specific cases. For details see Table 3.

Use of guidelines/proformas for CRC specimen reporting

Responders most commonly followed their national or local guidelines (n=59; 41.3%, excluding those who followed RCPath), RCPath (n=50; 35.0%) or CAP protocols (n=42; 29.4%) respectively, while RCPA was used by 1 responder (0.7%), and 4 responders (2.8%) didn't use any guidelines. 50 (36.2%) out of 138 European pathologists (n=138, 100%) used the RCPath guidelines, 60 (43.4%) national or local guidelines (excluding those who marked also RCPath), 37 (26.8%) the CAP protocol, while 4 (2.9%) didn't use any guidelines. 28 (n=28, 100%) UK pathologists followed the RCPath guidelines, while 22 (n=115, 19.2%) non-UK pathologists also used these guidelines. For more details see Table 3.

Discussion

Our study aimed to identify differences of existing CRC pathology reporting guidelines and to review local practice of pathologists in different countries, with the emphasis on whether and how local pathologists implement guidelines. To address these issues, a survey was sent out to pathologists practicing in different countries. Our survey shows that there is a wide variability among pathologists regarding which guideline they use and how strictly they follow individual recommendations in their daily practice. The differences we found are based on the fact that some data items were considered core or non-core, depending on the guidelines and that different TNM staging editions were recommended by different guidelines.

Interestingly, irrespective of the differences in the recommendations of the individual guideline, lymphovascular status was recorded by nearly all responders. This is reassuring, as LVI has been suggested as a prognostic factor for early-stage CRC and the presence of extramural vascular invasion is considered one of the high risk factors in stage II CRC with impact on adjuvant treatment decisions [29]. PNI was reported by 72% of responders. However, responders indicating to not report PNI, deviate from all the guidelines we reviewed except the SEAP guideline, which does not include this item. TB is currently reported (either "always" or "only when positive") by 70% of the responders and assessment methods applied by our responders differ. We believe, this is because the international standard on TB reporting has only been published recently [30]. TB is a non-core item, according to all the guidelines. It was found to be an independent predictor of lymph node metastasis in pT1 CRC and of survival in stage II CRC and can influence treatment decisions [29]. For the items, which are present in all or almost all of the analysed guidelines (LVI, PNI, TB or R margin status), we can identify non-compliers, as the percentage of responders, who never report certain item. For LVI it is 0%, as all the responders report it. When it comes to PNI, it is 4.2% and R margin status: 3.5%. For TB the percentage of those who don't report it is higher, mainly 28.7%, however, as mentioned above, the assessment was not standardized until recently. As these percentages are low, we could conclude that the compliance with guidelines is good. However, this criterium of evaluation can be somewhat controversial, as the total number of reported and omitted items should be analysed for each responder.

Another difference between CRC guidelines is the recommended staging system. RCPA, CAP, SEAP, and GIPAD/SIAPEC-IAP protocols were based on the AJCC or AJCC/UICC 7th edition of TNM [26], while RCPath and the Dutch guidelines were based on the Union for International Cancer Control (UICC) 5th edition of TNM [27].Therefore, to avoid confusion, the information on which TNM edition was used should always be included in the pathology report. Current RCPath and CAP guidelines have been updated with the 8th edition of UICC and AJCC TNM staging respectively [37-38]. Although the changes between the subsequent editions tend to be minor, Nagtegaal et al. highlighted how these modifications may affect the diagnosis and treatment decisions for CRC patients, using tumour deposits in pericolic fat as an example. There were different definitions throughout 3 editions (TNM5, TNM6, TNM7), which led to restaging of tumours, with a clear impact on the number of patients selected for chemotherapy [31]. This example shows how pathology reporting affects staging and therefore respective clinical decisions. Depending on the guidelines followed, patient could be staged with TNM 5th or 7th edition, which means potentially different treatment modalities.

Testing for microsatellite instability (MSI) is another issue where recommendations are currently not standardized across the guidelines. 63.6% responders declared different criteria for mismatch repair deficiency assessment, while 30.1% responders test all CRC. Universal testing is recommended by the newest guidelines of National Institute for Health and Care Excellence (NICE) [32] and the European Society for Medical Oncology (ESMO) guidelines [33]. The pathology datasets make reference to other guidelines, such as the revised Bethesda [34] or Amsterdam II criteria [35], therefore there is no unique approach. This item is important as it is prognostic for stage II CRC [29], potentially predictive for response to immune-checkpoint inhibitors in metastatic CRC [36] and is a screening tool for Lynch syndrome [32].

It is interesting to reflect on why there are differences between the national guidelines. We believe that these could be dictated by specific health care needs and standards of treatment in each country. They also depend on the standard procedures and protocols that define guidelines development, such as guidelines for authors of datasets of RCPA [39], and these can differ across countries. The differences depend also on who the stakeholders are and on their input in the guidelines, e.g. RCPath guidelines are consulted with five different organisations, among others, British Society of Gastroenterology or National Cancer Research Institute. Finally, different evidence levels scales serve as a reference for different guidelines. RCPath dataset is based on levels of evidence modified from Palmer K et al.[40]. RCPA and CAP use National Health and Medical Research Council (NHMRC) levels of evidence as a reference [39] , while SEAP guidelines are based on other national guidelines, such as CAP protocols, RCPath or RCPA datasets. GIPAD guidelines refer to other evidence scale, however the source is not indicated in the text. Generally, core items are supported by strong evidence from scientific literature. When this is not the case, it is the expert consensus which decides on the relevance of including the item [39]. As the national experts are different in each country, it is only logical that their consensus may differ from that of their colleagues in other country.

Although in our survey we focused on CRC surgical resection specimens only, it is worth mentioning that the pathology reporting guidelines also describe handling of local resections. There is a section dedicated to local excision in: RCPath, CAP, SEAP and GIPAD guidelines. The minimal data included in the report of local excision is similar to that of the resection specimen, however there is a number of specific features that need to be addressed. These are prognostic factors used for risk assessment of potential lymph node metastasis, distant metastasis and survival. They determine the necessity of a more radical surgical resection. These factors are: tumour size, poor differentiation, the depth of invasion into the submucosa, submucosal lymphatic or venous invasion, positive resection margin and TB [3-4,21-22].

In conclusion, we compared different CRC pathology reporting guidelines used around the world and conducted an international survey. Our intention was to highlight differences among these guidelines and review how these were implemented in the local practice of pathologists.

To our knowledge, this is the first survey that focused on clinical practice of local pathologists and reached responders from different countries. Our survey shows that there is a gap between CRC pathology reporting guidelines and everyday pathology practice raising the question, how compliance with guidelines can be improved. We believe, it is not a matter of updating the guidelines, that would reinforce the adherence to them. It is awareness of the clinical importance of individual items that could improve the compliance to the guidelines and the quality of the pathology report. This could be achieved by closer cooperation between specialists from different clinical areas, e.g. by joint scientific sessions or tumour boards. Regular audits of local pathology practice seem to be a potential way of reinforcing the adherence to the guidelines [41]. Whatever the differences in the guidelines are, they serve the same purpose: to set up the standards of pathology reporting in order to produce quality data for patient prognosis and management. Each of the guidelines we studied provides a template or a checklist to ensure the inclusion of important items. This approach is evidence-based, as use of proformas in pathology reporting have improved completeness of pathology reports [42,43]. Ideally, such proformas would be agreed internationally. This universal approach is represented by International Collaboration on Cancer Reporting (ICCR), which consists of representatives from major pathology organizations and its goal is to create internationally standardized and evidence based datasets for the pathology reporting of cancer [44]. The ICCR CRC dataset, however, is still in the process of development. Whether the publication of an international CRC dataset would eradicate the problem of guideline deviations remains to be seen. However, following a single international standard would have several advantages. One of the main beneficiaries would be patient management and clinical research. As clinical trials often take place in different countries and the data is collected from sites and centralized, the best solution to retrieve and analyse the data is to assure that they are in accordance to internationally approved guidelines. This is particularly important in pathology, where the diagnosis depends on the guidelines, as entities names and classification are constantly being updated. It would ensure use of consistent terminology and correct interpretation of data.

On the other hand, one can argue that a universal approach has also its shortcomings. The development of international guidelines can be disposed to limitations in terms of policies and available procedures in different countries. Also the economic issues create a gap between developing countries and economically stable countries. The resources would not allow certain countries or institutions to perform certain procedures, like molecular testing. Therefore the unified guidelines would have to consider these limitations. The solution could be a basic dataset, focused only on clinically relevant items, such as risk factors and items with a high level of evidence.

A limitation of our study was the missing data of a number of responders and the small size of subgroups (e.g. by nationality), which didn't allow comparative analysis. Therefore, no statistically significant associations were found. However, we believe the results are valid and should be made available to the public, as they address an important issue. We also found it impossible to directly link certain practice items to the guidelines, as in some cases the responders followed more than one type of guidelines. The generic term "national / local guidelines", did not allow us to know exactly which national or local guidelines the responders referred to in their answers. Moreover, the number of reviewed guidelines was limited. The study was also affected by the update in RCPath and CAP protocols, as the survey was performed before their release. However, in our opinion, this is a valid study, with the survey results compared to the recommendations available at that time.

In summary, we presented the variability of guidelines on CRC pathology reporting and the differences in adherence to these at a level of local practice. We believe that it is important to highlight these discrepancies among national guidelines and their local implementation because of their direct impact on patient management. This snapshot of real life practice should challenge pathologists to perform critical review of their local practices, develop a strategy for harmonization and raise the standards of quality in pathology.

Compliance with Ethical Standards:

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Contributions: Maria Urbanowicz, Heike I Grabsch and Jean-François Fléjou conceived and designed the study, and wrote, edited and reviewed the manuscript. All authors researched and analysed data, and wrote, edited, reviewed the manuscript and gave final approval for publication. All authors take full responsibility for the work as a whole, including the study design, access to data and the decision to submit and publish the manuscript.

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Table 1. Differences in CRC surgical specimen pathology guidelines and their clinical significance.

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	RCPath	RCPA	CAP	SEAP	GIPAD	Clinical significance
FIXATION TIME of CRC RESECTION SPECIMEN	24h	overnight	N/A	24-72h	N/A	Full fixation crucial for high quality pathology and increases lymph node yeld [1].
LYMPH NODE (LN) MACROSCOPICAL ASSESSMENT	Whole LN inclusion when <4mm, representative when >4mm diameter	Whole inclusion of macroscopically negative LN. Representative slide when macroscopic involvement.	Whole inclusion of macroscopically negative LN. Representative slide when macroscopic involvement.	N/A	N/A	Positive correlation between number of retrieved lymph nodes from patients with stage II and III CRC and survival [2]. Positive nodes determine adjuvant treatment [1].
SAMPLING METHOD OF POST NEOADJUVANT RESECTION SPECIMEN, with no visible gross tumour	addressed	N/A in detail	N/A in detail	N/A	N/A in detail	Tumour regression assessed by pathologic examination associated with better prognosis [3].
RESPONSE TO NEOADJUVANT THERAPY	4-tiered	4-tiered	4-tiered	4-tiered	3-tiered	Tumour regression assessed by pathologic examination associated with better prognosis [3].
LYMPHOVASCULAR /SMALL VESSEL INVASION (LVI)	NC**	C (intra- vs extramural)	C	C (intra- vs extramural)*	NC (except extramural venous invasion)*	associated with lymph node metastases and independent adverse prognostic factor [4]. vascular or lymphatic invasion is a high risk factor in stage II CRC patients, adjuvant treatment recommended [5].
VENOUS INVASION	C (deepest level)	C (intra- vs extramural)	NC ***	C (intra- vs extramural)*	C for extramural, NC for intramural*	Extramural VI independent adverse prognostic factor and risk factor for liver metastasis [6]. Vascular or lymphatic invasion is a high risk factor in stage II CRC patients, Adjuvant treatment recommended [5].
PERINEURAL INVASION	NC	NC	C	N/A	NC	Independent adverse prognostic factor [7]. A high risk factor in stage II CRC patients, Adjuvant treatment recommended [5].
TUMOR BUDDING	NC	NC	N/A	NC	NC	Independent predictor of lymph node metastasis in pT1 CRC and of survival in stage II CRC [8].
HIGHEST LYMPH NODE STATUS	C	N/A	N/A	N/A	N/A	Used for Duke's staging [9].
MAXIMUM DISTANCE OF TUMOUR SPREAD BEYOND MUSCULARIS PROPRIA (in mm)	C	NC	N/A	N/A	N/A	Depth of invasion prognostic (pT3 subdivision of added prognostic value) [10].
COMPLETENESS OF RESECTION AT MARGINS (RECORDED AS "R" STATUS)	yes	yes	no	yes	no	Margin involvement is a factor in risk assessment when considering adjuvant treatment in CRC [5]. Circumferential margin status predicts local recurrence in rectal cancer [11].
TNM EDITION	TNM5 UICC	TNM7 AJCC	TNM7 AJCC	TNM 7 AJCC/UICC	TNM 7 AJCC/UICC	The same tumour potentially having different stage depending on TNM edition, e.g. tumour deposits. Different treatment modalities [12].

* items from the checklist of minimal data
** refers to lymphatic vessels
*** NC to specify if venous, however suggested to report separately from small vessel invasion
C: core item, NC: non-core item, N/A: not addressed

Table 2. Survey on colorectal cancer (CRC) pathology reporting guidelines and local practice - profile of the responders.

Characteristics	Pathologists (n=143)
Specialization within pathology, n(%)	
Gastrointestinal	76 (53.1)
General Pathology	64 (44.8)
Other	3 (2.1)
Membership in organization, n(%)*	
EORTC	8 (5.6)
ESP	82 (57.3)
National Society of Pathology	123 (86.0)
Gastrointestinal pathology specialized organization	47 (32.8)
Not a member of any society	5 (3.4)
Workplace, n(%)*	
University Hospital	95 (66.4)
General Hospital	35 (24.5)
Private Practice	14 (9.7)
Cancer Center	19 (13.3)
Missing data	3 (2.0)
CRC resection specimens reported per year by institution, n(%)	
0-50	16 (11.2)
50-199	56 (39.2)
200-399	54 (37.8)
400-599	12 (8.4)
Over 600	5 (3.4)

* Multiple answer question

EORTC - European Organisation for Research and Treatment of Cancer, ESP - European Society of Pathology, CRC - colorectal cancer

Table 3. Survey on colorectal cancer (CRC) pathology reporting guidelines and local practice - questions and answers.

Resection specimen handling	**Pathologists (n=143)**
Do you receive the CRC resection specimen fresh, n(%)	
Yes, all	58 (40.6)
Only rectal resection specimens	10 (7.0)
No	71 (49.7)
Missing data	4 (2.7)
Inclusion of the proximal and the distal margins of the resection specimen in paraffin blocks, n(%)	
Yes	111 (77.6)
No	27 (18.9)
Missing data	5 (3.5)
Inclusion of the whole lymph node in paraffin blocks irrespective of its size, n(%)	
Yes	97 (67.8)
No	42 (29.4)
Missing data	4 (2.8)
Microscopic evaluation of CRC resection specimen	Pathologists (n=143)
Assessment of lymphovascular invasion status, n(%)	
Always	131 (91.6)
Only when positive	10 (7.0)
Never	0 (0)
Missing data	2 (1.4)
Assessment of perineural invasion status, n(%)	
Always	103 (72.0)
Only when positive	32 (22.4)
Never	6 (4.2)
Missing data	2 (1.4)
Assessment of tumor budding, n(%)	
Always	52 (36.4)
Only when positive	48 (33.6)
Never	41 (28.7)
Missing data	2 (1.3)
Assessment of residual tumor status (R) at the resection margin, n(%)	
Always	118 (82.5)
Only in rectal carcinoma specimens	15 (10.5)
Sometimes	3 (2.1)
Never	5 (3.5)
Missing data	2 (1.4)
Grading / staging systems	Pathologists (n=143)
Do you base cancer differentiation grading on the most prevalent component, n(%)	

Yes	107 (74.8)
No	27 (18.9)
Missing data	9 (6.3)
Primary tumor grading system used, n(%)	
2-tiered (low-grade vs high-grade)	43 (30.1)
3- or 4-tiered	97 (67.8)
Missing data	3 (2.1)
TNM edition used, n(%)	
TNM5	34 (23.8)
TNM6	1 (0.7)
TNM7	50 (35.0)
TNM8	55 (38.5)
Missing data	3 (2.0)
Other staging systems, apart from TNM, n(%)	
Yes	42 (29.4)
No	92 (64.3)
Missing data	9 (6.3)
Additional techniques	Pathologists (n=143)
MSI testing on CRC, n(%)*	
Always	43 (30.1)
When MSI-H phenotype on HE	54 (37.8)
In patients with a known family history of Lynch Syndrome	49 (34.3)
Upon request from clinicians	80 (56.0)
For the purpose of clinical research	22 (15.4)
Never	1 (0.7)
Missing data	8 (5.6)
MSI testing method, n(%)	
IHC only	79 (55.2)
IHC and, when loss of expression, PCR for confirmation	44 (30.8)
Always both IHC and PCR	11 (7.7)
PCR only	6 (4.2)
Missing data	3 (2.1)
Testing of any of the following: KRAS, NRAS, BRAF, PIK3CA or PTEN on CRC, n(%)*	
Always	8 (5.6)
In stage IV, metastatic or recurrent disease	33 (23.1)
Upon request from clinicians	112 (78.3)
For the purpose of clinical research	17 (11.9)
Never	8 (5.6)
Missing data	7 (4.9)
Molecular testing performed, n(%)	
In your department	75 (52.4)

In another laboratory	65 (45.5)
Missing data	3 (2.1)
Guidelines on CRC reporting	Pathologists (n=143)
Templates for cancer reporting, n(%)	
Yes	100 (69.9)
No	34 (23.8)
Missing data	9 (6.3)
Integration of template in local laboratory informatics system, n(%)	
Yes	73 (51.0)
No	39 (27.3)
Don't use templates	24 (16.8)
Missing data	7 (4.9)
Guidelines for CRC pathology reporting used, n(%)*	
RCPath	50 (35.0)
RCPA	1 (0.7)
CAP	42 (29.4)
National/local	71 (49.7)
No guidelines	4 (2.8)
Missing data	7 (4.9)

CRC - colorectal cancer, MSI – microsatellite instability, MSI-H - MSI-high, RCPath - the Royal College of Pathologists, RCPA - the Royal College of Pathologists of Australasia, CAP - the College of American Pathologists

Figure 1

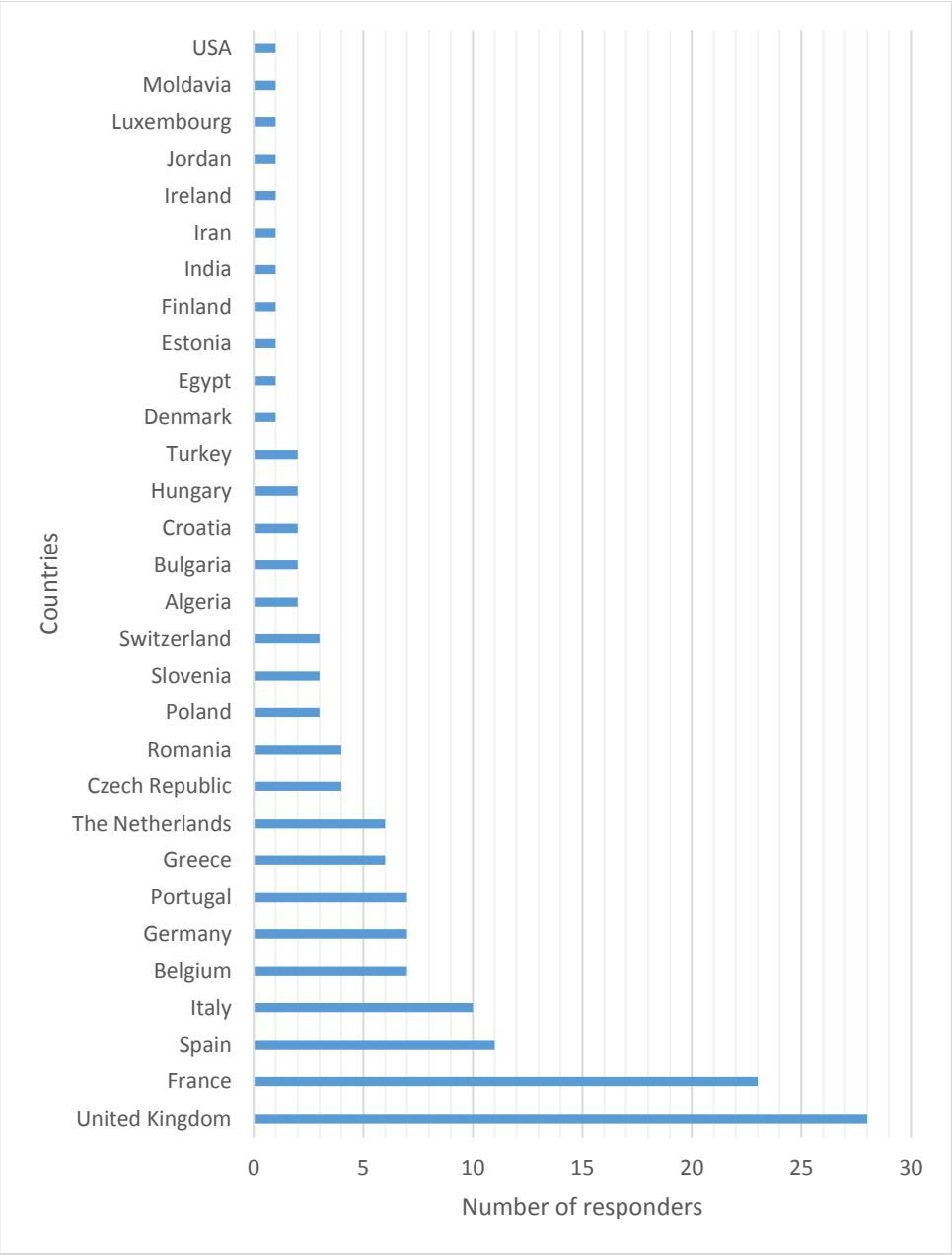

Fig. 1 Countries participating in the CRC pathology reporting survey

Figure 2

Gastrointestinal pathology specialized organization	Number of responders
Belgian Group of Digestive Oncology (BGDO)	1
Belgian Society of Gastrointestinal Endoscopy	1
British Society of Gastroenterology (BSG)	11
Club de Patología Digestiva SEAP	1
Club d'Histopathologie Digestive et Hépatique	5
European Association for the Study of the Liver (EASL)	2
European Network of Gastrointestinal Pathology (ENGIP)	8
European Society for Medical Oncology (ESMO)	1
Fédération Francophone de Cancérologie Digestive (FFCD)	1
Gastrointestinal External quality assurance (GI EQA)	1
Gastrointestinal Pathology Working Group of ESP	5
Gruppo Italiano Patologi Apparato Digerente and Società Italiana di Anatomia Patologica e Citopatologia Diagnostica (GIPAD-SIAPEC)	4
Rodger C. Haggitt Gastrointestinal Pathology Society (GIPS)	1
Société Française d'Hépatologie (AFEF)	1
Société Royale Belge de Gastro-Entérologie	1
Tertiary reference center	1
The European CanCer Organisation (ECCO)	3
The European Neuroendocrine Tumor Society (ENETS)	1
The International Society for Immunohistochemistry and Molecular Morphology (ISIMm)	1
United European Gastroenterology (UEG)	1

Fig. 2 Members of gastrointestinal pathology specialized organization