Variation in diagnosis, treatment and outcome in colon and rectal cancer

Elferink, M.A.G.

Chapter 5

Discussion

The survival rate of patients with colorectal cancer varies considerably across Europe. While the 5-year relative survival rate among patients diagnosed in the period 1995-1999 was 54% for the whole of Europe, it ranged from 39% to 60% between countries, with the Netherlands recording one of the highest rates, namely 57%.[1] Further improving this survival rate requires better understanding of the factors that influence the quality of colorectal cancer care. In the Netherlands, evidence-based multidisciplinary guidelines provide recommendations for diagnosis and treatment of colorectal cancer patients. Although it is generally accepted that guidelines adherence is important in delivering high quality care and focus on the uptake of guidelines is considered a useful strategy to improve outcome, until now there is a remarkable scarcity of data underpinning this assumption.

In this thesis we investigate the variation in diagnosis, treatment and outcome among patients with colon and rectal cancer in the Netherlands and evaluate guidelines adherence and outcome of colorectal cancer treatment using data from the Netherlands Cancer Registry.

Variation in staging and treatment

Under the premises that the guidelines concerning diagnosis and treatment of colorectal cancer would be widely accepted, we evaluated staging and treatment of colorectal cancer patients. The results of our studies as described in this thesis demonstrate large variations in staging and treatment between different healthcare providers and we conclude that the guidelines were not being followed in a large proportion of patients.

Staging

The first step in optimal treatment planning for patients with colorectal cancer is adequate staging, including staging of the primary tumour and regional lymph nodes, as well as excluding or confirming the presence of distant metastases. Uniformity regarding staging procedures is necessary in order to enable correct comparisons of treatment results obtained by different hospitals (e.g. for benchmarking), to evaluate if patients received proper treatment according to national standards, and to evaluate trends in outcome over time. Consequently, one of the objectives of this thesis was to assess the quality of lymph node evaluation in colorectal cancer by analysing the number of evaluated lymph nodes.

For accepting the N0 status, a minimum of 10 evaluated lymph nodes is required according to the Dutch guidelines for colorectal cancer. However, our studies demonstrated

that, in the period 2000-2006, this was achieved in less than 50% of the patients. As a consequence, positive lymph nodes might have been missed, which may have had consequences for the choice of adjuvant treatment after primary surgery. In order to define policies to improve the quality of lymph node evaluation, it is important to identify factors that contribute to inadequate lymph node staging.

For both rectal and colon cancer, large variations between individual pathology laboratories and hospitals were found. The median number of evaluated lymph nodes among rectal cancer patients ranged from 4 to 11 lymph nodes between pathology laboratories and, among colon cancer patients from 4 to 15 lymph nodes. Earlier studies had already reported on variation in lymph node evaluation.[2;3] In this thesis we also report a large inter-institutional variation in the number of evaluated lymph nodes. We used a multilevel analysis to investigate the variation between hospitals and pathology laboratories. The main advantage of this analysis is that it takes into account the hierarchical structure of the data. Other studies analysed either the variation between hospitals or the variation between pathology laboratories. With this multilevel analysis, the existing hierarchical structure of pathology laboratories serving one or more hospitals and hospitals operating on several patients with colorectal cancer could be analysed and variation between both hospitals and pathology laboratories was demonstrated. Our results showed that variation on the hospital level remained present after adjustment for the variation on the pathology laboratory level both among colon cancer patients and rectal cancer patients, indicating that both surgeons and pathologists should play a role in increasing the proportion of patients in which a sufficient number of lymph nodes is evaluated. Collaboration between these two disciplines is necessary to improve lymph node evaluation and we suggest that surgeons and pathologists should give feedback to each other about their performance. A surgeon could contact the pathologist when less than 10 lymph nodes are evaluated and a pathologist could contact the surgeon when the extent of the resected specimen is inadequate.

The adherence to national guidelines may be influenced by numerous factors. In this thesis, the focus was mainly on the possible influence of type and volume of pathology laboratories and hospitals. Our results showed that adherence for lymph node evaluation was higher in university pathology laboratories and university hospitals than in non-teaching pathology laboratories and non-teaching hospitals. The median number of evaluated lymph nodes was highest for university pathology laboratories and university hospitals. Furthermore, patients diagnosed in university hospitals whose lymph nodes were evaluated in university pathology laboratories were more likely to have 10 or more lymph nodes evaluated. This could be related to the supervision of the work of pathology residents in academic pathology laboratories, which means that residents receive

feedback about their work when an inadequate lymph node evaluation is performed. Another explanation could be the workload. Harvesting and analysing lymph nodes is a labour-intensive and time-consuming process and lack of time has been reported as barrier to adequate lymph node evaluation.[4]

Adequate staging implicates better alignment of treatment. Similar to other studies,[5-7] we reported an association between a low number of evaluated lymph nodes and a worse survival. This can be explained by understaging due to an incorrect classification of patients with a low number of evaluated lymph nodes as node-negative. If a higher number of lymph nodes was evaluated, some of these patients might have been categorized as node-positive. However, the association between the number of evaluated lymph nodes and survival was also found in node-positive patients, indicating that other factors also play a role in the difference in survival. A possible explanation is that it reflects the differences in the biological behaviour of the tumour and host and patients with a low number of evaluated lymph nodes might be patients with a reduced immune response to their cancer, leading to smaller lymph nodes that are more difficult to detect.[8;9]

Apart from understaging, inadequate lymph node evaluation can also lead to incorrect treatment choices among patients with colon cancer. According to the national guidelines, adjuvant chemotherapy should be considered for colon cancer patients with positive lymph nodes since there might be a survival benefit.[10] Due to an inadequate lymph node evaluation, positive lymph nodes might be missed, leading to undertreatment and worse survival. In addition, inadequate lymph node evaluation can also cause overtreatment among colon cancer patients. Adjuvant chemotherapy should, according to the guidelines, also be considered for high-risk stage II patients, including patients with an insufficient number of evaluated lymph nodes. Consequently, inadequate staging might infer avoidable chemotherapeutic treatment, which in itself is a considerable burden for patients and might induce serious adverse effects. Furthermore, it might lead to the inappropriate spending of health care budget.[11]

Treatment

In the current thesis, we demonstrated large variations between individual hospitals in the administration of (neo-)adjuvant therapies. These findings agree with previous results reported by others.[12;13] The proportion of rectal cancer patients with T2/T3-M0 tumours who received preoperative radiotherapy ranged from less than 50% to 100% and the proportion of colon cancer patients with positive lymph nodes who received adjuvant chemotherapy varied from less than 50% to more than 90% between individual hospitals. The question that arises is how these differences can be explained.

Deviations from the guidelines by the medical specialist may be due to several patient-related factors. In a survey among oncologists, performance status was identified as a factor influencing the choice of treatment.[14] Furthermore, patient preference has to be taken into account. In addition, older patients and patients with comorbidity have a higher risk of developing treatment-related complications leading to a worse survival.[15] Like several studies that showed that elderly patients and patients with comorbidities received adjuvant therapies less frequently,[12;16;17] the studies in this thesis also demonstrate that elderly patients are less likely to receive (neo-)adjuvant treatment. There are several explanations for this, such as impaired general condition of the patient and increased patient refusal.[18;19] In general, medical oncologists agree with the recommendations in the national guidelines for adjuvant chemotherapy for the relatively young and healthy patients with stage III colon cancer, but differ widely on recommendations for patients who are older and sicker.[20] Consequently, the likelihood of the more frailty elderly patients receiving adjuvant chemotherapy depends on the attitude and opinion of individual medical specialists. However, elderly patients can, like younger patients, also benefit from adjuvant chemotherapy.[21;22] Moreover, elderly patients who survive the first year after diagnosis have a similar prognosis compared to middle-aged persons.[23] Therefore, it should be stressed that deviation of the guidelines for an individual patient does in itself not necessarily mean worse quality of care, since non-adherence might be appropriate, tailor-made medical practice for an individual patient. Individualised treatment plans are needed in these situations, leading to good quality of care for individual patients. In general, however, treatment according to the guidelines is associated with good care. Differences between hospitals could be explained by differences in patient-mix, e.g. with regard to the presence of comorbidities. As a consequence, useful comparisons between hospitals require additional information on performance status, comorbidity and the reasons of deviating from the national guidelines.

This thesis found differences between hospital types and volumes in the administration of (neo-)adjuvant treatment. Patients diagnosed in teaching or university hospitals were less likely to receive (neo-)adjuvant treatment: rectal cancer patients diagnosed in teaching or university hospitals were less likely to receive preoperative radiotherapy compared to patients diagnosed in non-teaching hospitals and colon cancer patients diagnosed in teaching and university hospitals were less likely to receive adjuvant chemotherapy. Explanations could be that teaching and university hospitals have more patients with an impaired condition or with comorbidities or that these hospitals use a more strict selection of patients for (neo-)adjuvant therapies. However, hospital type and volume could not account for all variation. Variation within categories of hospital type and volume was also found suggesting the influence of other factors as well.

Neoadjuvant chemoradiation was introduced in the Netherlands around 2004. This thesis found large differences between CCC-regions in introducing this new therapy for patients with T4 rectal tumours, identifying slow and fast adaptors of changes in the guidelines between CCC-regions and indicating differences between CCC-regions in implementation and evaluation of guidelines. A review analysed the effect of several implementation strategies, such as educational materials and meetings, on the use of several guidelines with different topics.[24;25] Further research could determine which implementation strategies are most effective with regard to adapting new treatments.

Further research

At the hospital level, best practices should be identified and analysed for factors that determine why some hospitals perform better than others. Quality of care involves numerous aspects and instead of focusing on one indicator, the focus should be on a combination of indicators covering the entire process. The effect of innovations, such as clinical pathways, multidisciplinary meetings and case management, need further investigation. For several diseases an improvement in guidelines adherence was demonstrated due to the implementation of clinical pathways,[26-28] so it would be interesting to investigate whether these pathways can achieve the same effects in the care for colorectal cancer patients. The role of multidisciplinary meetings also needs to be explored. The care process of diagnosis and treatment of colorectal cancer patients is becoming increasingly complex, requiring expertise and skills from different relevant medical disciplines in a multidisciplinary meeting. This raises the question: what is the effect of discussing patients in a multidisciplinary meeting on treatment according to the guidelines? While in many hospitals in the Netherlands postoperative multidisciplinary meetings for colorectal cancer patients have been introduced, advances in neoadjuvant treatment and the need for meticulous preoperative analysis of the imaging results suggest that a preoperative multidisciplinary meeting might be very useful, especially for rectal cancer patients. A reduction of the variation in treatment due to multidisciplinary meetings had previously been demonstrated in breast cancer care.[29;30] Case management is often used to improve access and coordination of care. A trial among women with breast cancer revealed more appropriate treatment due to case management by specialized nurses,[31] suggesting it could also reduce the variation in colorectal cancer care.

Using data of the NCR

All the studies in this thesis used data from the NCR. This has several advantages. Due to thorough training of the registration clerks and a quality control system at a national

level, the quality of the data is high.[32] Furthermore, being a population-based registry, it provides data from an unselected patient population. On the other hand, the main limitation of the NCR is that information for a more accurate evaluation of the guidelines adherence is not available. For example, information about case-mix, such as performance status, comorbidity and setting (acute versus planned operation), is essential when adherence to the guidelines between hospitals is compared. Furthermore, it would be interesting to extend the analyses about guidelines adherence at the institution level and evaluate the guidelines adherence by individual surgeon, pathologist and medical team. Unfortunately, information at the level of medical specialists is lacking in the NCR.

Complete and validated registration of all relevant items for evaluating guidelines adherence is required because without such registration, accurate benchmarking between hospitals will be hampered and will not allow for correct comparisons between hospitals. Collection of such data is, however, labour-intensive and requires adequate and additional support from data management and information and communication technologies.

Outcome

Besides affecting guidelines adherence, numerous previous studies analysed the relation of (hospital or surgeon) volume and specialisation with outcome.[33-35] Several studies reported an inverse association between hospital volume and outcome, especially for high-risk operations such as esophagectomy and pancreatectomy.[33;36;37] Others demonstrated a similar relation between surgeon volume and outcome.[34;38] For colorectal cancer, this association is not that clear.[39-42] In addition, a high-volume hospital does not necessarily mean a high volume per surgeon, but depends on the number of surgeons in a hospital. Some studies investigated the interaction between hospital volume and surgeon volume. An American study demonstrated that hospital volume could be used as a surrogate for surgeon volume in improving outcome, because the degree of the outcomes of hospital volume and surgeon volume were comparable.[43] Another study analysed data from the Surveillance, Epidemiology and End Results (SEER)-Medicare database and suggested that in colon cancer, hospital volume may have a stronger effect on outcome than surgeon volume, while in rectal cancer, surgeon volume was a more important determinant.[44;45] We were, however, not able to investigate the effect of surgeon volume, because data on the surgeon level were not available on a national basis in the NCR. A study using data from the cancer registry of the north-eastern region in the Netherlands found an association between higher surgeon volume and better disease free survival, but no effect of surgeon volume on the overall survival.[46]

Our studies revealed an inverse relationship between hospital volume and postoperative mortality for rectal cancer patients, but not for colon cancer patients, possible because rectal cancer surgery is more complex and technically more demanding than colon cancer surgery. The lower postoperative mortality in high-volume hospitals might reflect the specialised and more experienced surgeons in these hospitals which is needed for rectal cancer surgery.[47] One multicenter study reported lower intra-operative and postoperative complication rates in high-volume hospitals.[48] Similar to other studies,[45;49-51] our study showed differences in overall survival between hospital types and volume, especially for colon cancer. Our finding that colon cancer patients diagnosed in university hospitals have better survival rates and are less likely to receive adjuvant chemotherapy seems to be contradictory and we do not have a proper explanation for this result.

Centralisation

It is often suggested that referral of patients to high-volume hospitals with highly specialized medical teams improves quality of (colorectal) cancer care. Due to the complex treatment required for T4 rectal tumours and local recurrences of rectal cancer, the Dutch guidelines recommend centralizing the surgical treatment of these tumours in specialised centres with sufficient expertise. They also advise that transanal endoscopic microsurgery (TEM) should only be performed in hospitals with adequate facilities and expertise.[52] Therefore, hospitals have to make adequate referral appointments depending on requested facilities and expertise according to the guidelines. There should be no large variation in quality of care between hospitals that provide colorectal cancer care. Hospitals should improve their quality of care by analyzing the whole care process and using a benchmark of multiple indicators covering the entire process which enables hospitals to compare their results with the results of other hospitals. This provides better insight into aspects, which could be improved. Hospitals are also likely to improve their practice when their performance is worse than other hospitals.

Feedback

Our studies on lymph node evaluation showed considerable improvement in adequate lymph node evaluation over time. When more lymph nodes are evaluated, more patients with positive lymph nodes are detected. This means that improvement of lymph node evaluation leads to more accurate treatment choices. The improvement over time might be an effect of the feedback to all pathology laboratories based on the results of the TME-trial. A population-based study in the south of the Netherlands suggested that individual feedback to medical specialists in multidisciplinary working groups may have played a role in the increase in number of evaluated lymph nodes.[11] All feedback has led to an increased awareness of the importance of a sufficient number of evaluated lymph nodes for an accurate decision on treatment and an adequate prognosis.

Several previous studies demonstrated an improvement in quality of care due to feedback of individual results to medical specialists.[53-55] A review of the Cochrane Collaboration revealed that audit and feedback can be effective in improving professional practice, especially when adherence to recommendations is low at start and when feedback is more intensive.[56] Some European countries, such as Sweden, Norway, Denmark and the UK have an audit for (colo)rectal cancer.[57-60] In the Netherlands, the Dutch Surgical Colorectal Audit (DSCA) started in 2008, aiming to provide reliable, case-mix adjusted, quality information to individual providers to improve their performance.[61] Since then nearly 20.000 patients have been entered in the database. The DSCA was initiated by medical specialists. This enhances the willingness of medical specialists to participate in the audit compared to their willingness to participate in a measure of an external organization, such as the Health Care Inspectorate. Clinical information about patients with colorectal cancer is collected in the hospitals by medical specialists. A large amount of information is registered, allowing monitoring of the whole care process instead of focussing on one factor. Since, by participating in the DSCA, hospitals show their active role in quality improvement, the Health Care Inspectorate has chosen participation in the DSCA as an indicator since 2009. However, only information about surgical patients, focusing on the surgical treatment, is collected. To monitor the whole multidisciplinary care process of colorectal cancer patients, the registration should be extended to collecting information about all colorectal cancer patients and involving other disciplines. As this collection of data also implies an administrative burden for medical specialists, the use of this information should be optimized and collaboration with existing databases, such as the NCR, is required to verify the quality of the data, include additional information to the database and avoid duplication of registration. In a few years time, the effect of the audit should be related to the effects on outcome, as can be achieved in a collaborative approach by the DSCA and the NCR.

Introduction of mass screening

In recent decades, treatment strategies for patients with colorectal cancer have changed repeatedly. In rectal cancer care, the total mesorectal technique (TME) technique has replaced conventional blunt dissection, leading to a decreased local recurrence rate.[62;63] In addition, there was a shift from postoperative radiotherapy to preoperative radiotherapy and neoadjuvant chemoradiation was introduced for patients with locally advanced rectal cancer. The benefit of adjuvant chemotherapy for colon cancer patients with positive lymph nodes is well established, while the role of adjuvant chemotherapy among patients with stage II disease is still unclear. Due to further advances in chemotherapy agents in more recent years,[64-66] there was a considerable increase in the administra-

tion of adjuvant chemotherapy among patients with stage III disease and, to a lesser extent, among patients with stage II disease as shown in our results. Studies in this thesis showed that these changes in treatment coincided with an improvement in survival for both colon and rectal cancer in the period 1989-2006.

Further improvement in survival of colorectal cancer could be achieved by implementing a screening program, provided the participation rate is high. Since colorectal cancer has a long premalignant stage, which is easily detectable and can be treated properly, a screening program is very suitable for colorectal cancer. Some European countries are gradually implementing a national screening program for colorectal cancer, e.g. the United Kingdom and Finland.[67;68] In the Netherlands, the Dutch Health Council has advised the government to start with colorectal cancer screening using biannual iFOBT (immunochemical faecal occult blood test) for persons aged 55-75 years.[69] Introduction of screening will lead to an increase of precursor and early stages leading to a more favourable stage distribution and a reduction in disease-specific mortality.[70-72] The Dutch Health Council has calculated that annually more than 1400 deaths due to colorectal cancer could be prevented if the participation rate is 60%.[69] Another benefit of the screening is avoidance of the development of colorectal cancer. Faecal occult blood testing also reduces the risk of developing colorectal cancer due to detection and removal of adenomatous polyps or adenomas.[73] This will lead to a decrease in the incidence of colorectal cancer. However, the introduction of a screening program will increase the workload for, among others, endoscopists and pathologists, because a colonoscopy will be performed in all patients with a positive FOBT test. Due to insufficient colonoscopy capacity and financial reasons, the minister of Health, Welfare and Sport postponed the decision about the introduction of colorectal cancer screening to 2019.

Conclusion and recommendations

The research for this thesis was undertaken to identify factors influencing quality of care and outcome by investigating the variation in guidelines adherence (staging and treatment) and perceived outcome of patients with colon and rectal cancer in the Netherlands. Considerable variation between hospitals and pathology laboratories in adequate lymph node evaluation was revealed leading to suboptimal staging and potentially inaccurate treatment plans and large differences between hospitals were found in treatment according to the guidelines. To optimize the quality of care and thus outcome, this variation in staging and treatment should be reduced. Based on the results of this thesis, it can be concluded that a part of the variation is associated with type and volume

of hospitals and pathology laboratories. However, the large variation between individual hospitals suggests that these characteristics do not account for all variation. High-volume or teaching status is no guarantee for high quality of care. Hospital type and volume are only proxy measures for other factors leading to improved quality of care, with some individual low-volume hospitals providing good care and some individual high-volume hospitals providing suboptimal care. Furthermore, some variation in treatment could be explained by differences in case-mix. Therefore, case-mix adjusted information related to outcome is required for a more accurate analysis.

To obtain targets for improvements, further research is required to identify other factors causing the variation between individual hospitals. Several aspects, such as clinical pathways, multidisciplinary meetings, case management and implementation strategies, could be analysed to determine whether these are associated with the differences in performance between hospitals. Revealing best practices is likely to generate new standards which could be used in benchmarking. Decisions on centralisation of certain treatments or differentiation of tasks of medical specialists should preferably be based on these comparisons.

Quality of care is complex and comprises numerous aspects. To improve outcome by optimizing the quality of care, it is important to analyse the whole care process. Focussing on only one factor is insufficient and is no guarantee for high quality of care. A range of indicators (process, structure and outcome) is necessary to monitor the whole care process. The medical specialists, including all relevant disciplines, should determine this set of indicators allowing them to indicate which aspects are important and should be benchmarked. Health care insurances and the Health Care Inspectorate could use this set to assess the quality of the care. Continuously monitoring the whole care process will provide insight to the medical specialists in the different aspects of care that could be improved. This requires reliable information which could also be of benefit for patients and other organizations in health care, such as health care insurances and the Health Care Inspectorate. Providing insight into the differences in patterns of care and outcome between medical specialists and hospitals could lead to an improvement in quality of care. A reliable performance registration combined with essential case-mix information is required to make this comparison.

It is therefore recommended that:

- Regular monitoring and feedback to the medical specialists about indicators, which were defined by the professionals themselves, should be organized;
- Continuous improvement should be pursued by continuously monitoring the care process, identifying best practises and implementing and evaluating these best practices;

– Other factors influencing quality of care should be explored and best practices should be revealed.

In conclusion, large variation between hospitals and pathology laboratories was demonstrated in adherence to the guidelines of diagnosis and treatment for patients with colon and rectal cancer in the Netherlands. This is associated with type and volume of hospitals and pathology laboratories. However, not all variation could be explained by these characteristics. Therefore, continuous monitoring is necessary to give feedback to medical specialists, identify best practices and analyse factors which influence quality of care and outcome.

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