Quality indicators in head and neck oncology

de Ridder, M.

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CHAPTER 9

Summary, discussion and conclusions

SUMMARY

CHAPTER 1.
GENERAL INTRODUCTION OF THE THESIS

This thesis describes the search for quality indicators in head and neck oncology. The National Healthcare Institute of the Netherlands states that aging of the population will lead to an increased pressure on the Dutch healthcare system in 2030[1]. Taken into account the costs of all healthcare innovations, especially in the field of oncology, a challenge lies ahead to still treat every patient according to the highest standard in decades from now. Obviously, current high standards should not be compromised and quality of care must be clearly defined. The first step to define current quality is to develop a set of indicators for the assessment of quality.

In order to structure the assessment of quality of care, Donabedian et al.[2] subdivided quality of care into three indicator pillars: structure, process and outcome. All three components are not only separately involved in assessment of quality, but also related to each other. Structure indicators describe the health care setting in which care is provided (hospital type, numbers of qualified personnel and hospital volume). Process indicators measure the process of diagnosis and treatment on a patient level and are based on evidence from literature or consensus between experts. Outcome indicators denote the actual outcome of treatment. This can be evaluated by a broad spectrum of measurements ranging from undesired events during treatment (complications, incomplete resections) to survival of patients and quality of life scores using validated questionnaires.

The main objective of this thesis is to explore currently available information on variation in care and possible quality indicators in head and neck cancer care and derive lessons for future studies and quality evaluations.

CHAPTER 2.
VOLUME CRITERIA FOR THE TREATMENT OF HEAD AND NECK CANCER: ARE THEY EVIDENCE BASED?

It is already known from other low-volume high-risk fields of oncology (for instance esophageal and pancreatic cancer treatment) that provider or procedural volume relates to outcome. The purpose of this literature review is to evaluate the volume-outcome relationship in head and neck cancer care.
Our literature search led to the inclusion of eight published papers on the volume-outcome relationship in head and neck cancer. All eight studies describe a positive relationship; increased provider or procedural volume leads to improved survival.

Several comments can be made in relation to the volume-outcome literature:

1. Outcome measures should be clinically relevant. Sometimes 30-days mortality is chosen as outcome parameter for high-risk surgical procedures, whereas 30-days mortality of head and neck cancer procedures is typically low.
2. Volume is often presented as a categorical variable, where volume actually needs to be analyzed as a continuous variable. There is also much heterogeneity of cut-off points presented in literature.
3. Case mix is an important factor when analysing results of different hospitals. Many studies lack adequate adjustment for differences in case-mix between providers.
4. Head and neck cancer is a group of distinct cancer types with all (subtle) different treatment options and outcome. To consider head and neck cancer as one group in volume-outcome studies can cause under-/overestimation of the effect on individual head and neck cancer subsites.

Despite all limitations, all reviewed papers point towards a positive volume-outcome relationship. Definitely more research needs to be done to further characterize this relationship with emphasis on case mix adjustment and tumor specific volume effects.

CHAPTER 3.
VARIATION IN HEAD AND NECK CANCER CARE IN THE NETHERLANDS - A RETROSPECTIVE COHORT EVALUATION OF INCIDENCE, TREATMENT AND OUTCOME.

Head and neck cancer consists of a heterogeneous group of cancers. As a group it is the 9th most common cancer type. However, all subtypes can be viewed as low incidence tumors. Since the foundation of the Dutch Head and Neck Oncology Collaborative Group in 1984, head and neck cancer is treated predominantly in eight specialized head and neck centers or one of the six preferred partner hospitals across the country. The aim of this study was to evaluate variation of care in the Netherlands.
A large (n=2094) retrospective (2008) nationwide cohort of patients with head and neck squamous cell carcinoma was identified in the Netherlands Cancer Registry. The variation in numbers, treatments and treatment results between 7 tertiary head and neck cancer centers and 3 preferred partner clinics across the Netherlands was studied. The number of new head and neck cancer patients varied from 129 to 417 between the head and neck cancer centers. The numbers per center of the more rare cancer types (nasopharynx, nasal cavity, salivary gland) were less than 10 patients per year in nearly all centers. Types of treatment and outcome varied between the centers especially in oral cavity and oropharyngeal cancer. In oral cavity cancer there was for instance diversity in the use of postoperative radiotherapy (18% to 40%) and survival varied significantly. In oropharyngeal cancer there was variation in the amount of patients treated with organ preserving therapy [i.e. (chemo-) radiotherapy] with a range of 65 to 85% per center and survival differed significantly between the hospitals. For laryngeal cancer there were no statistically significant differences between the hospitals regarding treatment and outcome.
In the total cohort of head and neck cancer patients a significant volume-overall survival relation was found, stratified for age, sex and stage, since the hazard of dying was 0.98 (95% CI) for every increase with 25 patients per year.
From this study, we concluded that there was interhospital variation in 2008 in treatment for oropharynx, oral cavity, hypopharynx cancer, but not for larynx cancer. The numbers of the more rare cancer types (nasopharynx, salivary gland and paranasal sinus) were too low per hospital for meaningful analyses.

CHAPTER 4.
THE ASSOCIATION OF TREATMENT DELAY AND PROGNOSIS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC) PATIENTS IN A DUTCH COMPREHENSIVE CANCER CENTER

Waiting time is one of the most psychologically distressing parts of the whole process from symptoms to diagnosis and treatment. In this study we evaluated the association between treatment delay and long-term outcome for head and neck squamous cell carcinoma in a Dutch tertiary head and neck cancer center.
We retrospectively studied a cohort of 2,493 HNSCC patients of the Netherlands Cancer Institute (NCI), diagnosed between 1990-2011. Professional delay was categorized into three categories: referral, diagnostic and total treatment delay.
The median time from diagnosis to treatment was 39 days (25-75% inter quartile range: 26.5 – 51), and it was found that year of diagnosis (early period), tumor site (oral cavity) and type of therapy (surgery) were all statistically significant of influence on the delay. We also found that referral time (time from biopsy elsewhere to first visit at NCI) significantly increased over time (from 10 – 13 days).
In the multivariate Cox proportional regression analyses performed, we found that patients with a treatment delay of less than 30 days had a higher risk of dying from the head and neck tumor [HR 0.82 (95% CI: 0.70–0.95)].
In sub-analyses this effect was independent from tumor (stage) or patient (age, sex) characteristics. An explanation could be that the early treated (<14 days) patients were selected by the physician to start early because of a biologically more aggressive tumor (history of tumor growth or more complaints of pain). In this study population prolonged waiting did not negatively influence survival.

CHAPTER 5.
THE INFLUENCE OF NODAL YIELD IN NECK DISSECTIONS ON LYMPH NODE RATIO IN HEAD AND NECK CANCER

The occurrence of cervical lymph node metastases is one of the most important prognostic factors in head and neck cancer. In the currently used TNM-staging, lymph node metastases classification is based on diameter, bilateral occurrence and number of positive nodes. In order to optimize prognostication, the concept of lymph node ratio was introduced. The lymph node ratio is calculated by dividing the number of positive nodes by the total number of harvested lymph nodes at a neck dissection. This ratio determines the extent of cancer spread, but also the extent of clearance.
The purpose of this study was to investigate the influence of nodal yield in neck dissections on the lymph node ratio.

The focus was on the influence of change in specimen processing at the pathology department on lymph node yield and lymph node ratio. The protocol of specimen processing encompassed a change in 2007: pathologists harvested the lymph nodes themselves before 2007, thereafter pathology technicians were involved.
This change in protocol resulted in a significantly higher yield of lymph nodes after 2007 (24 vs. 32, $p<0.001$), with a stable number of positive lymph nodes (1.9 vs. 2.1, $p=0.519$), leading to a decline in LNR. This increased number of lymph nodes was partly explained by an increased number of lymph nodes found in level V. Literature, as well as this study, confirmed that level V contains many (small) lymph nodes. The total number of lymph nodes decreased significantly after pre-operative (chemo-) radiotherapy, from a mean of 31 in patients without pre-operative treatment to 20 after radiotherapy or even 18 after (chemo-) radiotherapy ($p<0.001$).
This study showed that standardization of pathology processing is an important quality indicator before interpretation of the prognostic value of LNR.

CHAPTER 6
A CRITICAL EVALUATION OF LYMPH NODE RATIO IN HEAD AND NECK CANCER

The previous study (chapter 5) showed that lymph node ratio is strongly dependent on the protocol of specimen processing. The aim of this study was to investigate the influence of this protocol change on the prognostic value of lymph node ratio.
Only patients with cervical lymph node metastases were included. Those with a conglomerate of lymph nodes (N3 disease) were excluded because lymph node ratio is less reliable in those patients. Also patients who have been previously treated with radiotherapy on the neck were excluded, because total lymph node harvest in previously irradiated patients is significantly lower[3].
In total 176 patients with positive nodal HNSCC were studied. We performed survival estimate analyses on two time periods, based upon a switch in pathology processing protocol. This switch caused an increased yield of lymph nodes and a stable amount of positive lymph nodes found in neck dissection specimens. The lymph node ratio was calculated for both periods and the prognostic value was evaluated.
In the multivariate analyses it was found that pN-stage was an equally potent or even better prognosticator than the LNR. This can be explained by the earlier finding of the denominator variation of the ratio (total number of harvested lymph nodes) and a stable numerator (total number of positive nodes). To set a quality standard and to be able to reliably compare hospitals regarding lymph node dissections a minimum of lymph nodes need to be examined, like for instance in colon carcinoma.
It can be concluded from this study that without standardization of specimen processing LNR is unreliable as prognosticator. Total number of harvested lymph nodes should be used as quality indicator instead.

CHAPTER 7

AN EPIDEMIOLOGICAL EVALUATION OF SALIVARY GLAND CANCER IN THE NETHERLANDS (1989-2010) - TRENDS IN SALIVARY GLAND CANCER

Salivary gland carcinomas are a special group among head and neck carcinomas, because of the very low incidence, a great variation in histopathological subtypes and the lack of "classical head and neck" risk factors.
The aim of this study was to evaluate the progress made in salivary gland cancer over the past 22 years. Data was extracted from the Netherlands Cancer Registry, resulting in 2737 patients with a primary salivary gland carcinoma.
Trends over time in incidence and mortality were evaluated by calculating estimated annual percentage changes over the European Standardized Rates (ESR).
Incidence remained stable around 0.7 per 100,000. Most of the tumors (78%) originated from the parotid glands. Surgery (with or without radiotherapy) was treatment of choice in 84% of the cases. Over time the use of adjuvant radiotherapy increased (~6%).
Adenocarcinoma was the most common histological type, followed by squamous cell carcinomas, acinic cell carcinomas, adenoid cystic carcinomas and muco-epidermoid carcinomas. Striking differences were found between sexes. Mortality tended to increase in men over the years, whereas in women it remained stable. Also the 5-year relative survival was lower for men (63%) compared to women (76%). This effect could be partly explained by the higher initial tumor stage and/or by the higher proportion of poorly differentiated adenocarcinomas (with worse prognosis) in men.
We concluded that there has been barely any progress made in treatment of salivary gland cancer over the past 22 years.

CHAPTER 8
SALIVARY GLAND PLEOMORPHIC ADENOMA IN THE NETHERLANDS: AN OBSERVATIONAL NATIONWIDE STUDY OF PRIMARY TUMOR INCIDENCE AND RECURRENCE RATE.

The majority of the salivary gland tumors is benign of origin. Of the benign salivary gland tumors, pleomorphic adenomas are the most frequent. Pleomorphic adenomas are known for their ability to transform from benign to malignant, so-called carcinoma ex pleomorphic adenoma. Literature on the occurrence of pleomorphic adenoma, recurrence rate after surgery and primary or secondary malignant transformation is only available from single institution series. National data is hard to retrieve in the Netherlands, since its Cancer Registry only registers malignant tumors. So for this study, we used the nationwide pathology database PALGA.
From PALGA, excerpts of all patients that have had a pleomorphic adenoma since 1992 (16,437 patients) were retrieved. Data from this database is not coded and consists of free text, which had to be hand-coded to be able to perform analyses. For that reason we depicted 5 incidence years (1992, 1997, 2002, 2007 and 2012, representing in total 3506 patients) as a representative sample of possible pleomorphic adenomas and performed trend analyses on this data.
We found that the European standardized incidence rate of pleomorphic adenoma in 2012 in the Netherlands was 4.7 per 100,000 (total number of patients: a little less than 800 per year). The incidence of pleomorphic adenomas in women rose over the years with 1% per year, whereas it remained stable in men.
The long-term risk of (histology proven) recurrence was 4.6% for first recurrence. This percentage increased steeply for second, third etc. recurrence. Malignant transformation was very rare (1%) and transformed recurrences were not seen in our cohort. To define risk factors for recurrence we performed a multivariable analysis: lower age at diagnosis and positive or uncertain resection margins were associated with risk of recurrence.
This study is the first to give an accurate overview of nationwide incidence and recurrence of pleomorphic adenoma. Statistically significant risk factors for recurrence were identified, like positive or uncertain surgical margins, younger age at primary diagnosis or primary pleomorphic adenoma in the parotid gland.

DISCUSSION

Driven by the public's attention and demand for transparency, quality assessment in medicine has become increasingly important during the last decades. The vast expansion of health care innovations forces administrations to make deliberate choices on organization and evaluation of care to secure optimal quality and cost effectiveness of treatments. This makes quality of care currently a key factor in all healthcare policies in the Western world. One of the challenges is to deal with the dilemma how to keep quality high for all patients in light of increasing demands that stem from demographic and societal developments. In several fields of medicine like surgical oncology and cardiovascular surgery major progress has been made using quality assessment as a tool for increasing quality of services. For instance, the New England cardiovascular project reduced the mortality rate (minus 24%) of coronary artery bypass surgery by a structured program of visits, data sharing and training[4]. Also in cancer care, several quality improvement programs or initiatives started up in the last decade. In the Netherlands, the Dutch Pancreatic Cancer Group was formed in 2010, aiming at multidisciplinary collaboration in research, guideline development and they also introduced a nation-wide prospective audit (Dutch Pancreatic Cancer Audit; DPCA)[5]. In the audit detailed clinical data are collected of all patients with pancreatic cancer in whom surgery is performed in the Netherlands, to provide clinicians with timely, actable and benchmarked feedback information to improve the quality of their care process and outcomes. In addition, this collaboration resulted in several multicenter trials and further improvement in pancreatic cancer care. For upper gastro-intestinal tract cancer an identical group was formed, the Dutch Upper GI cancer group (DUCG)[6]. Their mission is to improve quality of care in upper GI cancer patients by supporting multidisciplinary clinical and translational research and support in patient registries. In contrast, the head and neck cancer counterpart, the Dutch Head and Neck Audit (DHNA), is relatively new and does not have published results yet.

Factors that determine quality

As mentioned in the introduction of this thesis, quality is hard to capture. The multi-dimensional and, in case of head and neck cancer, multidisciplinary character, makes it hard to define it in concrete terms. Many medical specialists, each of them with specific super-specialized expertise, are responsible for a (small) part of the process (i.e. head and neck surgeon, radiation oncologist, medical oncologist, radiologist, pathologist, nuclear physician). Added thereto the involved paramedics (i.e. nursing staff, speech pathologist, dietician and physical therapist) make it even harder to define the process of quality assessment. To create more clarity in the field of quality, Donabedian et al. in 1988[2] developed a model of quality indicators categorized in three components: structure, process and outcome.

Structure indicators

Procedural volume – on a hospital or surgeon level - is one of the most frequently studied, though also one of the most controversial structure indicators. "Practice makes perfect" may be a strong argument, especially in surgical disciplines, but is it sufficiently strong to explain the volume-outcome relation? As mentioned in the introduction, almost all literature regarding the volume-outcome relations in high-risk and or low-volume care shows a positive association[7-11]. A supplementary explanation for this could be that several (infrastructural) factors (like the function of a tumor board, efficiency of the infrastructure between different services or training of paramedics for instance) are better organized in high volume hospitals than in low volume hospitals. This volume effect will probably be more outspoken in countries with non-centralized head and neck cancer care.

Although many studies pointed to a logical correlation between volume and outcome for high risk – low volume care, it is still necessary to define a minimum number of procedures. Compared to the North American counterparts like Memorial Sloan Kettering Cancer Center, MD Anderson, UCSF, Princes Margaret Toronto and Johns Hopkins, all Dutch head and neck cancer centers are low volume centers with mean volumes of ±250 new patients per year[12]). Taking into account the differences between the Dutch centers and American Cancer Centers, it is remarkable that each of these US head and neck cancer centers surpasses the number of 4000 new patients per year[13-16], compared to the total of 3000 new patients per year in the Netherlands, who are treated in eight different head and neck centers [or one of the six preferred partners]. This indicates a high level of efficiency and cost effectiveness in these US centers. This high standard of head and neck cancer care attracts many second opinions from all over the world, which can be seen as a quality indicator by itself. Although there are very few standardized outcome measures to compare head and neck cancer centers internationally. Moreover, it should be realized that these large cancer centers are also exceptional in the US and that a large proportion of head and neck cancer patients are treated in general hospitals, with larger differences in hospital volumes in the US than in the Netherlands.

Measured by European standards the level of head and neck cancer care in the Netherlands is high and according to the survival analyses in the EUROCARE-5 studies one of the best in Europe[17]. Despite the variation in care as described in chapter 3, this leading position in Europe can be attributed to the well-organized care in tertiary head and neck cancer centers, national treatment guidelines and standardized multidisciplinary approach in each of these centers.

Variation of care and guideline adherence

Evidence-based guidelines are tools meant to guarantee the same basic knowledge regarding the best treatment options available for medical teams in all hospitals. Adherence to guidelines is often used as process indicator with the assumption that overall a more evidence-based care process leads to better patient outcomes. Guidelines standardize treatment and set standards of care. Variation of care should not be confused with variation in quality of care. Guidelines leave room for variation to optimize treatment in individual cases in certain circumstances. A striking example in this respect is the treatment of T1 laryngeal cancer. The Dutch guideline states that endoscopic treatment is comparable to radiation in oncologic outcome as well as functional outcome. In such a case, specific expertise of the head and neck team and patient preferences will cause variation in care that is according to the guideline.

Adherence to guidelines can serve as surrogate marker for differences in quality of care and few studies evaluated adherence to guidelines and its effect on outcomes for the head and neck cancer setting[5, 6, 18, 19]. A study evaluating the protocol compliance of radiotherapy plans for advanced head and neck cancer patients, showed that 25% of the plans were incompliant[6]. For patients planned to receive over 60 Gy (curative dose) with major deficits in the treatment plan, it was found that survival significantly declined (5-y survival 50% vs. 70%). Of note, major deficiencies in the treatment plan were highly correlated to low volume hospitals ($p<0.001$)[6].

The volume-guideline adherence relationship was reproduced by Eskander et al.[19] in a cohort of 5720 surgical head and neck patients. They observed a guideline adherence of around 75%. Several recommendations of the guideline were evaluated, like head and neck imaging, chest imaging, multidisciplinary meetings and follow up. Higher hospital volume and even higher surgeon volume were significantly associated with better guideline adherence ($p<0.001$). The influence of guideline adherence on outcome was also demonstrated in a Dutch retrospective study[18] evaluating over 800 head and neck cancer patients eligible for curative treatment. It was found that 17% of the patients did not receive guideline compliant therapy. Ten percent was due to incompliant advice by the tumor board and the other 7% due to patients' preferences. Patients receiving non-standard treatment due to incompliant advice had significantly lower overall survival after 3y (HR 2.1 – 95% CI 1.49-3.03). Since guidelines encompass the best evidence based treatment for specific patients the outcome of the study might not be surprising, however, if we combine the aforementioned study results, it is striking that most probably 10-15% of the head and neck cancer patients had a two times higher risk of dying within three years due to guideline incompliance.

PROCESS INDICATORS

The counter effect of increased volume can be prolonged waiting times for diagnostics or treatment. Waiting time (or treatment delay) makes patients feel insecure and nervous[20]. And due to possibly rapid tumor growth in head and neck cancer, there is a rationale for research on waiting times as quality indicator. A clear definition and method to measure treatment delay (day of first visit – first day of treatment) make it a potentially strong indicator. In other sites (uterine[21] and breast[22] for instance) the effect of treatment delay on outcome was already shown. In head and neck cancer, however, the literature was not clear on this point. Our study of 2400 patients[23] showed that patients treated with the shortest treatment delay had the worst survival. This effect, called the waiting time paradox, is explained by confounding by indication (patients with rapid progression or extreme symptoms are treated first). The larger population-based study by van Harten et al.[24] (over 13,000 patients), however, showed the negative impact on survival of prolonged treatment delay. They found a curve describing hazard ratio of dying that rapidly ascends from 0-25 days of delay, followed by a plateau until two months and after two months another rapid ascend. The cutoff point formulated by the Dutch head and neck collaborative group (NWHHT) of 30 days was not found to be significant in this study.

One of the options to shorten waiting times is to implement short-track programs, like all diagnostics and tumor board meeting on one day. Currently several head and neck cancer centers are implementing or have implemented such a program. One of the conditions necessary for short track programs combined with higher volume care is optimal logistics without increasing the costs extraordinarily.

Optimizing logistics is also at stake in the chain of surgery and specimen processing. First is the issue of the extent of the lymph node dissection. The more (fatty) tissue is removed, the more lymph nodes will be found. Therefore neck dissections should be performed in a standardized fashion[25] and taking into account the anatomical boundaries of the neck levels. When surgery is performed according to these guidelines, variance in the extent of surgery will be limited. Training institutions should focus on the adherence to surgical guidelines, supervised by independent audit committees composed of professionals. This brings us to the last part: the specimen processing at the pathology department. Should the pathologist try to find, evaluate and describe every node present in the specimen? There is growing literature about the (prognostic) value of the lymph node ratio (LNR) in various surgical fields [26, 27]. LNR represents the ratio between total number of positive lymph nodes and total number of harvested lymph nodes. This last mentioned part of the lymph node ratio is critical. The total number of removed lymph nodes roughly depends on three factors. The first is the variable number of neck nodes; it is known that total number of lymph nodes varies considerably between humans[28].

However, this variation is indefinable since surgery is not standardized and specimen processing is not standardized.
We found that the introduction of a different specimen processing protocol changed the results in the number of lymph nodes found in dissection specimens[29, 30]. If calibration scales differ between two centers, results cannot reliably be compared anymore.
Another critical step in the diagnostic (and/or treatment) trajectory is the pathology report. Synoptic pathology reporting can be part of an improvement strategy, incorporating only important and crucial information in a standardized fashion. This can act as a sort of scale calibration, provided that a uniform acquisition of input is guaranteed (in our study for instance, the protocol of specimen processing).
Standardized (synoptic) pathology reports result in more complete reports on pathology, more consistency of the reports and also in quicker available and unambiguous information[31]. This will make it easier for clinicians to adhere to guidelines and possibly lead to a minimization of treatment delay, increase the efficiency of multidisciplinary tumor boards and also increase the quality of (retrospective) research. Another possible solution to improve the process is to combine efforts of maxillo-facial surgeons and otorhino-laryngologists working in the field of head and neck cancer to set up uniform training schedules and head and neck oncology departments, solely dedicated to the diagnosis and treatment of this disease. Apart from the logistic benefits this will also contribute to savings of costs, time and energy.
These are just examples, and nearby future research needs to focus on how to develop an efficient workflow.

Outcome indicators

Especially in case of "orphan" head and neck cancers like salivary gland, nasopharynx and paranasal sinus cancer, the field demands a major step forward. For nasopharyngeal[32] and paranasal sinus carcinomas[33] the lack of improvement in survival is shown in literature. As we have demonstrated in this thesis, the current centralization rate for salivary gland carcinomas does not lead to volumes with enough power for research on quality or improvement of outcome (some centers only saw 3 new patients in 2008). We demonstrated a lack of improvement in outcome over the past 22 years for salivary carcinomas, most probably due to the absence of effective (neo-adjuvant) systemic therapy[34]. A reason could be that randomized clinical trials are almost impossible to initiate, if there are no international collaborations to create enough statistical power. Centralization or redistribution of patients with salivary gland cancer, currently not surpassing 10 patients/year per center and representing more than 20 histological subtypes, seems almost inevitable and might contribute to a less fragmented participation in international collaborations in search for new treatment regimens.

A nice example of such international collaboration for rare tumors is seen in Ewing sarcomas within the framework of EURAMOS[35]. Ewing sarcomas are very rare soft tissue tumors (20-25 patients per year in the Netherlands, which are centralized treated in four specialized centers), where it was possible to perform a randomized trial comparing several treatment regimens[36] due to sufficient patient accrual across borders.
Such international collaborative initiatives may be the key for improvements in salivary gland cancer treatment. Of note, salivary gland cancer exist of much more different entities compared to Ewing sarcomas, thus it will remain hard to design and initiate randomized trials. Existing and proven effective, international collaborations, like the European Head and Neck Society (EHNS), International Federation of Head and Neck Societies (IFHNOS) or EORTC need to get together and initiate international (randomized) studies for these rare tumors.

Future improvement programs

A part of the above-mentioned indicators are currently included in a prospective audit of the Dutch Head and Neck cooperative group (NWHHT) that is being rolled out nation-wide[18]. A full set of multidisciplinary quality indicators has been developed by the Scientific Institute for Quality of Healthcare[37]. This audit will prospectively gather information on patient, tumor, treatment and hospital characteristics in all head and neck cancer centers in the Netherlands. The Dutch Head and Neck Audit (DHNA) is collaboration between the Dutch head and neck collaborative group (NWHHT), the Scientific Institute for Quality of Healthcare and the Dutch Federation for University Medical Centers.
The strength of clinical auditing lies in the total package it covers. It combines guideline adherence, case-mix differences and different outcome measures to give an overview of the current quality of care at specific hospitals. Benchmarking hospital-specific results catalyzes quality improvement[38]. Hospitals scoring well on certain indicators are challenged to keep their reputation on level and hospitals scoring worse on certain indicators are challenged to score as well as their bench marked partners. Conceptually beautiful, but hospitals need to be willing to be completely transparent. Our retrospective study on variation already showed that lack of transparency of hospitals could limit quality of care research; see chapter 3.

Transparency

Transparency is the key factor for quality improvement programs. Hospitals need to open up and show their results. As a hospital organization you can learn from others or others can learn from you on certain indicators, but you need to know the performance from each other. According to Wouters[39], transparency can be seen as a 7 level process (figure 1).

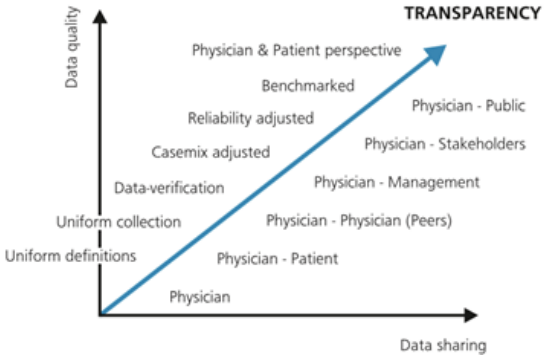

Figure 1. The seven level process of transparency

The spectrum of transparency starts with availability of trivial hospital specific outcome information and it ends with full publicly availability of hospital or physician specific outcome data. The goal of transparency is dual: for patients, so they are able to choose the best hospital for their treatment and for hospitals to create a transparent benchmarked situation so less performing hospitals know where to target their improvement efforts. The Dutch Institute for Clinical Auditing (DICA) has delivered the proof of concept[38] for comparing hospital-specific risk-adjusted indicator results, primarily to provide doctors with benchmarked feedback information, though also to make (differences in) quality of care transparent for all stakeholders.

The benefit of transparency disappears if the reporting of results is not correct. A hospital can publish superior results on their website, but if they are selective, manipulated or incorrectly gathered the benefit of transparency turns 180 degrees.

Austin et al.[40] described how to avoid pitfalls in five steps of quality measurement and reporting.

1. Measures must be developed and specified for the performance measured. If not, you are extrapolating or assuming, which decreases the quality of your data tremendously.
2. Data must be identified and collected to populate the measures. So you need to have a measurement specific quality assurance, in order to guarantee quality of the data.
3. Collected data must be applied to the measured specifications. An example in this respect is blood loss during surgery in ml. One surgeon measures it accurately, whereas the other surgeon makes estimates based on impression. This leads to variability and uncertainty in the collected data.

4. Public reports must be reliable regarding classification. Any predefined category must be reported concordantly. So "hospital A", must be "hospital A" in your dataset and "physician B", must be "physician B". This to prevent misclassification and thereby misinterpretation of the data.
5. Communicate results in such a way that there is no room for misinterpretation. Make sure your report for the press is written according to the knowledge level of the reader.

These five steps are visible in the approach of DICA and were taken into account at the foundation of the DHNA[29].

Value-based health care

Internationally there are several initiatives to transform health care from a volume-driven to an outcome-driven industry. According to Michael Porter, a healthcare economist from the Harvard Business School, providers should make patient value the overarching goal to keep high quality health care sustainable, especially in Western countries. Maximizing value for patients, means achieving the best outcomes at the lowest costs. This adds another dimension to the perception of (high) quality care described in this thesis. With the initiation of the DHNA the Dutch Institute for Clinical Auditing will provide the Head and neck cancer centers in the Netherlands with benchmarked feedback on their outcomes; clinical as well as patient reported outcomes. Head and neck cancer centers should use this information to learn from each other and start fine-tuning and individualizing their multi-disciplinary care processes. If also the costs of these care processes are measured and stay on the same level or show a relatively low increase, patient value will improve. In addition, better care processes may not only lead to better outcomes on the short term, though also long-term functional outcomes of patients may improve leading to less disabilities and better societal participation. The International Consortium of Health Outcomes Measurement (ICHOM) organizes global teams of physician leaders, outcomes researchers and patient advocates to define Standard Sets of outcomes per medical condition, and then drives adoption to enable health care providers globally to compare, learn, and improve their care [www.ichom.org]. By bringing health outcome measurement from a national to an international level, insight in variation in care processes and the resulting outcomes between providers in different countries could lead to even more improvement in patient value. An international standard set for measuring outcomes of Head and neck cancer patients is not available yet, though will certainly be developed in the near future.

Conclusion

This thesis shows the complexity and multidimensional concept of quality of care in head and neck cancer. The selected topics represent examples of quality assessment using structure [centralization (Chapter 2) and variation of care (Chapter 3)], process [waiting time (Chapter 4) and pathologic specimen handling (Chapter 5, 6)] and outcome indicators [influence of volume and variation of care on outcome (Chapter 3) and specific outcome of rare head and neck tumors arising in the salivary gland (Chapter 7, 8)].
Head and neck cancer care in the Netherlands is centralized in specific head and neck cancer centers, but nonetheless the care given varied per head and neck center. We showed that volume may play a role in this variation, but several other quality related aspects of head and neck cancer care are of influence as well. For instance: waiting time differences, as we showed that waiting time has significant influence on outcome. What we also showed is that pathology specimen handling is another key factor, and that non-standardized workflow leads to differences and non-uniformity.
For the more rare types of head and neck cancer, like salivary gland tumors, the low volume in the Netherlands makes quality assurance almost impossible. For proper quality assessment and thereby quality assurance, based upon this thesis, redistribution of rare head and neck cancers appears inevitable. The variation in numbers and treatment we found could have been biased by case-mix factors we did not include. The relatively small sample size of our study population limited us regarding some statistics. With data currently being gathered in the DHNA, more insights in the variation of care can be given. Especially on detailed, stage corrected treatment variation. Hopefully the prospective audit database (DHNA) will serve as a unique source of answers to quality of care questions and will give direction to further improvement of the (already) high quality head and neck cancer care in the Netherlands.

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9

SAMENVATTING (NL)

Hoofdstuk 1.
Algemene inleiding

Dit proefschrift beschrijft de zoektocht naar kwaliteitsindicatoren in de hoofd-hals oncologie. Door vergrijzing van de populatie en toegenomen behandelingsmogelijkheden door de vooruitgang in de medische wetenschap is er een verhoogde druk ontstaan op de zorginstellingen om iedere patiënt volgens de hoogste standaard te behandelen (zeker binnen de oncologie). Het is essentieel dat kwaliteit van zorg te allen tijde bewaakt wordt. De eerste stap in dit proces is om de huidige kwaliteit - en de mogelijke variatie tussen zorgaanbieders - vast te stellen door het identificeren van belangrijke kwaliteitsaspecten en het ontwikkelen van kwaliteitsindicatoren.
Om onderzoek naar kwaliteit van zorg te structureren hebben Donabedian et al.[1] indicatoren in drie categorieën verdeeld: *structuur, proces en uitkomstindicatoren*. Deze worden niet alleen afzonderlijk, maar ook in relatie tot elkaar onderzocht.
Structuurindicatoren beschrijven de zorgomgeving waarbinnen zorg wordt geleverd (ziekenhuistype, patiënten aantallen en beschikbaarheid van gekwalificeerd personeel).
Procesindicatoren beschrijven het zorgproces: het diagnostisch traject, de medische besluitvorming, de behandeling en de nazorg.
Uitkomstindicatoren beschrijven de daadwerkelijke uitkomst van een behandeling binnen een breed spectrum variërend van overleving van een groep patiënten tot een door de individuele patiënt ingevulde vragenlijst over kwaliteit van leven.
De inhoud van dit proefschrift richt zich op onderzoek naar actuele variatie van hoofd-hals oncologische zorg en identificatie van mogelijke kwaliteitsindicatoren om toekomstig onderzoek naar kwaliteit van zorg te sturen.

Hoofdstuk 2.
Volume criteria voor de behandeling van hoofdhalskanker: zijn deze "evidence based"?

Van andere 'laag volume – hoog risico' vormen van oncologische chirurgie, zoals slokdarm- en pancreaschirurgie is bekend dat volume per ziekenhuis of chirurg gerelateerd is aan uitkomst.
Wij onderzochten deze relatie aan de hand van acht gepubliceerde artikelen over de volume-uitkomst relatie bij hoofd-halskanker. In alle gevallen werd een positieve correlatie aangetoond tussen een hoger volume en een langere overleving.

Bij dit literatuuronderzoek werden een aantal kritische kanttekeningen gemaakt

1. Uitkomst is klinisch niet altijd relevant gemeten: in sommige gevallen werd gekozen voor sterfte binnen 30 dagen na chirurgie als uitkomst; voor hoofd-hals kanker patiënten is deze sterftemaat erg laag en zijn verschillen daardoor minder relevant.
2. Volume werd vaak weergegeven als categorische variabele, echter volume is een continue variabele en dient ook als zodanig te worden onderzocht. Bovendien is er veel variatie in afkapwaarden gebruikt in de beschreven literatuur.
3. 'Case mix-correctie' is een belangrijk onderdeel van vergelijkingen van uitkomsten van ziekenhuizen en veel studies missen correctie voor deze verschillen in "case mix".
4. Hoofd-halskanker is een verzamelterm voor verschillende subtypen kanker met (subtiele) verschillen in behandeling en uitkomst. Door hoofd-halskanker als één groep te beschouwen in de volume-uitkomst studies bestaat er een kans op onder- of overschatting van het effect.

Ondanks alle beperkingen wijzen alle onderzochte artikelen in de richting van een positieve volume-uitkomst relatie. Met zekerheid kan gezegd worden dat er meer onderzoek nodig is om deze relatie verder te karakteriseren, waarbij de nadruk moet liggen op gedegen correctie voor 'case mix' en verschillen tussen tumortypen.

Hoofdstuk 3.
Variatie van hoofd-hals oncologische zorg in Nederland – een retrospectief cohort onderzoek naar incidentie, behandeling en uitkomst.

Hoofd-halskanker bestaat uit een heterogene groep van aandoeningen. In Nederland is het de 9e meest voorkomende kankersoort. Individuele typen zijn ieder als zeldzame tumor te classificeren. Sinds de oprichting van de Nederlandse Werkgroep Hoofd-Hals Tumoren (NWHHT) in 1984 worden hoofd-halstumoren hoofdzakelijk behandeld in een van de acht hoofd-hals centra en zes zogenaamde 'preferred partners' verspreid over het land. Dit onderzoek richtte zich op variatie in hoofd-hals oncologische zorg tussen deze centra.
Er werd een retrospectief landelijk cohortonderzoek verricht van 2094 hoofd-halskanker patiënten, die geregistreerd zijn door de Nederlandse Kanker Registratie. De variatie in patiënten aantallen, behandeling en uitkomsten werd vergeleken tussen 7 hoofd-halscentra en 3 preferred partners. Het aantal patiënten per jaar in 2008 varieerde van 129-417 tussen de hoofd-halscentra. Voor de meer zeldzamere typen, zoals speekselklier-, nasofarynx-, neus - en neusbijholten carcinoom, was het patiënten aantal minder dan 10 patiënten per jaar voor bijna alle deelnemende centra.

Behandeling en uitkomstmaten varieerden voornamelijk bij het mondholte- en orofarynx-carcinoom. Voor het mondholte carcinoom varieerde de toepassing van postoperatieve radiotherapie per centrum van 18% tot 40%. Tevens was er een significant verschil in overleving waar te nemen. Voor het orofarynxcarcinoom was er variatie in het percentage patiënten dat orgaansparend behandeld werd (65% - 85%). Eveneens varieerde de overleving significant binnen deze patiëntengroep. Voor larynxcarcinoom patiënten werd er geen verschil in behandeling of uitkomst gevonden tussen de verschillende centra.
In het totale cohort werd er na multivariate analyse een significant volume-uitkomst effect vastgesteld na stratificatie voor leeftijd, geslacht en stadium. De hazard ratio (HR) voor overlijden was 0.98 per toename van 25 patiënten/jaar.
Geconcludeerd wordt dat er was van een significante variatie tussen ziekenhuizen in 2008 voor wat betreft de behandeling van orofarynx-, mondholte- en hypofarynxcarcinoom. De patiënten aantallen voor de zeldzamere hoofd-halstumoren, nasofarynx-,speekselklier-, neus- en neusbijholtencarcinoom, waren te beperkt om in de overlevingsanalyse mee te nemen. Over het algemeen was er een tendens waarneembaar van een positieve relatie tussen ziekenhuisvolume en overleving voor de totale groep van hoofd-halstumoren.

Hoofdstuk 4.
Het verband tussen wachttijd tot behandeling en prognose bij hoofdhalscarcinoom patiënten uit het Nederlands Kanker Instituut/antoni van leeuwenhoek.

Een lange wachttijd is voor veel patiënten een stress verhogende factor gedurende het proces van diagnose en behandeling. In deze studie werd het verband tussen wachttijd en overleving onderzocht in een retrospectief cohort van 2493 hoofd-halscarcinoom patiënten (1990 – 2011) van het Antoni van Leeuwenhoek (AVL). Wachttijd werd onderverdeeld in drie groepen: wachttijd in het verwijzingsproces, gedurende de diagnostiek en in het geheel van de totale behandeling.
De mediane wachttijd tussen diagnose en behandeling was 39 dagen (25-75% met een spreiding van 26.5 – 51 dagen). Drie factoren waren significant gecorreleerd aan een langere wachttijd: een vroeger tijdvak van behandeling, behandeling voor een mondholtecarcinoom en primaire chirurgie behandeling. Tevens werd vastgesteld dat de tijd die verloopt tussen biopt in een ander ziekenhuis en het 1e bezoek in het AVL in de loop der jaren significant is toegenomen, van 10 naar 13 dagen. In het multivariate Cox regressie model bleek dat patiënten met de kortste wachttijd van minder dan 30 dagen een hoger risico hadden om te overlijden aan het hoofd-halscarcinoom [HR 0.82 (95% CI: 0.70–0.95)]. In een sub analyse bleek dit onverwachte resultaat onafhankelijk van tumor stadium, leeftijd of geslacht.

Een aannemelijke verklaring hiervoor zou kunnen zijn dat deze patiënten een klinisch snel progressieve tumor hadden met snelle toename van klachten, die het behandelend team ertoe deed besluiten deze patiënten met voorrang te behandelen.
In deze studie bleek een langere wachttijd de overleving niet negatief te beïnvloeden. Toekomstig onderzoek zal zich richten op het onderzoeken van de relatie tussen wachttijd, psychologische stress en/of morbiditeit.

Hoofdstuk 5.
de invloed van lymfeklier opbrengst na halsklierdissecties op de lymfeklierratio in hoofd-halskanker.

De aanwezigheid van halskliermetastase(n) is een van de belangrijkste prognostische factoren voor overleving bij hoofd-halskanker. In de huidige TNM-classificatie worden lymfekliermetastasen geclassificeerd op basis van diameter, aantal en eenzijdig of dubbelzijdig voorkomen. In een poging het voorspellen van de prognose te verbeteren is het concept van de lymfeklierratio bedacht. Deze ratio wordt berekend door het aantal tumorpositieve lymfeklieren te delen door het totaal aantal verwijderde klieren. Hierdoor is niet alleen het aantal positieve klieren van belang, maar ook de uitgebreidheid van de chirurgische ingreep en het aantal lymfeklieren dat door de patholoog gevonden is in het verwijderde weefsel. Deze studie concentreerde zich op de invloed van de lymfeklieropbrengst na halsklierdissectie op de lymfeklierratio met focus op de invloed van een gewijzigd uitsnijprotocol van het operatiepreparaat. Het protocol hiervoor werd in 2007 gewijzigd, waardoor het niet meer de pathologen zelf waren die uitsneden, maar speciaal daartoe opgeleide laboranten. Dit resulteerde in een significant hogere opbrengst van totaal aantal lymfeklieren (24 vs. 32, $p<0.001$), met een stabiel aantal positieve lymfeklieren (1.9 vs. 2.1, $p=0.519$) met als gevolg een afnemende lymfeklierratio. Het toegenomen totaal aantal verwijderde lymfeklieren werd hoofdzakelijk verklaard door een toename van het aantal lymfklieren in level V. Het totaal aantal lymfeklieren daalde significant wanneer patiënten preoperatieve (chemo-)radiatie hadden ondergaan. Deze studie laat zien dat standaardisatie van het pathologie protocol een belangrijke kwaliteitsindicator is alvorens lymfeklierratio betrouwbaar kan worden geïnterpreteerd als prognostische factor.

Hoofdstuk 6.
Een kritische evaluatie van lymfeklierratio in hoofdhalskanker.

De studie voorafgaand aan deze studie (hoofdstuk 5) toonde dat lymfeklierratio sterk afhankelijk is van het protocol dat gebruikt wordt voor het uitsnijden van het preparaat. Deze studie richtte zich op de invloed van een uitsnijprotocolwijziging op de prognostische waarde van de lymfeklierratio. Hiervoor werden alleen patiënten met positieve hals lymfeklieren geïncludeerd. Patiënten met N3 ziekte en voorafgaande (chemo)radiatie op de hals werden geëxcludeerd vanwege onbetrouwbaarheid van de lymfeklierratio bij deze patiënten. In totaal werden 176 patiënten met positieve halsklieren van een hoofd-halscarcinoom geïncludeerd. Vervolgens werden er overlevingsanalyses gedaan voor de groep patiënten die voor en na de protocolwijziging zijn behandeld. Deze wijziging heeft tot een grotere opbrengst van lymfeklieren in het halsklierdissectiepreparaat geleid, zonder dat er extra metastasen werden gedetecteerd. In de multivariate analyse bleek pN-classificatie minstens even goed of zelfs beter voorspellend te zijn voor de prognose in vergelijking met de lymfeklier ratio. Dit kan verklaard worden door de eerder gevonden variatie in de noemer van de ratio (totaal aantal lymfeklieren) en een stabiele teller (aantal positieve lymfeklieren). Om een kwaliteitsstandaard neer te zetten en om tevens verantwoord te kunnen vergelijken tussen verschillende ziekenhuizen moet er een minimum gesteld worden aan het aantal
onderzochte lymfeklieren, zoals dat ook gedaan is bij het coloncarcinoom. Uit deze studie kan geconcludeerd worden dat zonder standaardisatie van de wijze waarop een hals-lymfeklierdissectiepreparaat wordt uitgesneden de lymfeklierratio als onbetrouwbare prognostische factor kan worden aangemerkt. Als kwaliteitsindicator kan beter het totaal aantal onderzochte lymfeklieren gehanteerd worden.

Hoofdstuk 7.
Een epidemiologische evaluatie van het speekselkliercarcinoom in Nederland(1989-2010).

Vanwege hun lage incidentie, grote variatie in histopathologie en het ontbreken van klassieke risicofactoren vormen speekselkliercarcinomen een speciale groep tumoren binnen het geheel van hoofd-halscarcinomen. Het doel van deze studie was om te evalueren welke vooruitgang er geboekt is in de afgelopen 22 jaar bij de behandeling van het speekselkliercarcinoom. Hiervoor werden er gegevens van 2737 patiënten met een primair speekselkliercarcinoom opgevraagd bij de Nederlandse Kanker Registratie.

Trends in incidentie en mortaliteit werden geëvalueerd aan de hand van geschatte jaarlijkse procentuele veranderingen in Europees gestandaardiseerde cijfers voor incidentie en overleving.
Incidentie bleef stabiel, rond 0.7 per 100,000 patiënten per jaar. De meerderheid van de tumoren (78%) ontstond in de glandula parotis. De meeste patiënten (84%) werden chirurgisch behandeld, met of zonder adjuvante therapie. In de loop der jaren werd er een toename van ongeveer 6% gezien in toepassing van postoperatieve radiotherapie. Qua histologie kwamen achtereenvolgens adenocarcinomen het meest voor, gevolgd door plaveiselcelcarcinomen, acinic cell carcinomen, adenoïd cysteus carcinomen en muco-epidermoïd carcinomen. Opvallende verschillen werden gevonden tussen beide geslachten. De mortaliteit leek toe te nemen over de jaren bij mannen, waar deze bij de vrouwen stabiel bleef. Daarbij was ook de 5-jaars relatieve overleving lager voor mannen (63%) dan voor vrouwen (76%). Dit effect kan deels verklaard worden door het hogere tumor stadium en een groter aandeel van slecht gedifferentieerde adenocarcinomen (met een slechtere prognose) bij mannen. Concluderend is er weinig vooruitgang geboekt in de behandeling en prognose van speekselkliercarcinomen gedurende de laatste 22 jaar. Wij zijn ervan overtuigd dat verdere centralisering en toegenomen 'awareness' voor speekselklier-zwellingen kunnen bijdragen aan betere uitkomsten.

Hoofdstuk 8.
Pleiomorf adenoom van de speekselklieren in Nederland: een observationele landelijke cohort studie van incidentie en recidief percentage.

De meerderheid van de speekselkliertumoren zijn benigne van aard. Van deze benigne tumoren zijn pleiomorf adenomen de meeste voorkomende. Het pleiomorf adenoom staat erom bekend dat het maligne kan ontaarden tot een carcinoom ex pleiomorf adenoom. Over de incidentie van pleiomorf adenomen, recidief percentage na behandeling en secundaire maligne ontaarding is alleen literatuur beschikbaar van beperkte ziekenhuis series. Vanwege het feit dat de Nederlandse Kankerregistratie zich alleen richt op de registratie van maligne tumoren zijn landelijke gegevens moeilijk te verkrijgen. Om die reden is er voor gekozen om data te verzamelen uit het landelijke PALGA systeem (Pathologisch-Anatomisch Landelijk Geautomatiseerd Archief). Van alle patiënten die vanaf 1992 met een pleiomorf adenoom werden gediagnosticeerd (n=16437) werden gegevens opgevraagd uit PALGA. Omdat de onderzoeksgegevens in vrije tekst opgenomen waren moesten deze daaruit worden gedestilleerd en met de hand gecodeerd worden. Daarom is besloten om 5 incidentie jaren (1992, 1997, 2002, 2007 en 2012) te selecteren resulterend in 3506 representatieve patiënten .

De Europees gestandaardiseerde incidentie in Nederland van pleiomorf adenomen in 2012 werd door ons vastgesteld op 4.7 per 100,000 (totaal aantal patiënten ongeveer 800 per jaar). De incidentie van pleiomorf adenomen bij vrouwen steeg met 1% per jaar, waar deze bij mannen stabiel bleef.
De lange-termijnkans op een (histologisch bewezen) eerste recidief was 4.6%. Dit percentage liep snel op voor de kans op tweede, derde en volgende recidief. Maligne ontaarding was met ongeveer 1% zeer zeldzaam. Tumorrecidieven transformeerden in ons materiaal niet tot een maligniteit. Aan de hand van een multivariate analyse bleken een lage leeftijd bij het stellen van de diagnose en positieve of onzekere resectie marges bij pathologisch onderzoek risico factoren voor een recidief te zijn.
Concluderend gaf deze studie een vrij nauwkeurig overzicht van de incidentie en recidief kans van pleiomorf adenomen in Nederland.

CONCLUSIES

Dit proefschrift beschrijft de complexiteit van het kwaliteitsconcept rondom hoofd-hals oncologische zorg. Het is een complex onderwerp, omdat de hoofd-halskanker zorg per definitie multidisciplinair is en omdat de kwaliteit van zorg vanuit verschillende invalshoeken benaderd kan worden. In de drie domeinen van kwaliteit van zorg, *structuur, proces en uitkomst*, werden verschillende indicatoren onderzocht. Binnen het domein *structuur* werd de centralisatie en variatie van zorg bestudeerd. Hieruit bleek dat, ondanks de hoge centralisatie graad, de variatie in volume en behandeling tussen de hoofd-hals centra significant verschillend was. In de literatuur wordt een verminderde adherentie aan de richtlijnen genoemd om deze variatie te verklaren met een negatieve invloed op de overleving van patiënten. Binnen het domein *proces* werd de invloed van wachttijd op overleving onderzocht. In de studie zoals opgenomen in dit proefschrift vonden wij een contra-intuïtieve uitkomst, namelijk dat patiënten met de kortste wachttijd ook de slechtste overleving hadden. Deze paradox lijkt verklaard doordat patiënten met snel progressieve tumoren of snel levensbedreigende symptomen als eerste behandeld worden. Uit een daaropvolgende landelijke vervolgstudie[2] bleek de negatieve invloed van langere wachttijd op overleving aantoonbaar. Aangenomen wordt dat wachttijd een belangrijke kwaliteitsindicator is in de behandeling van hoofd-halskanker patiënten. Naast de wachttijd werd er in dit proefschrift ook aandacht besteed aan de rol van geprotocolleerd uitsnijden van een halsklierdissectiepreparaat. Hoewel wij ons realiseren dat het aantal lymfeklieren in de hals verschilt per patiënt, beperkt gestandaardiseerde chirurgie logischerwijs de variatie in aantallen. Door een wijziging in uitsnijprotocol van een halsklierdissectiepreparaat vond men significant meer lymfeklieren in het preparaat, terwijl het aantal tumor positieve lymfeklieren gelijk bleef.

In de literatuur beschrijven verschillende series de prognostische waarde van de ratio tussen tumor positieve lymfeklieren en het aantal verwijderde lymfeklieren in de hals. Dit wordt de lymfeklierratio genoemd. Door niet gestandaardiseerde chirurgie of pathologie wordt zo'n ratio volstrekt onbetrouwbaar en niet universeel toepasbaar als prognostische factor. Verdere concentratie van hoofd-halsoncologische zorg kan hier een positieve bijdrage aan leveren Binnen het domein *uitkomst* focust dit proefschrift op een van de meer zeldzamere vormen van hoofd-halskanker, het speekselkliercarcinoom. Uit ons onderzoek blijkt dat er in de afgelopen 22 jaar weinig tot geen verbetering in overleving wordt gezien. Bovendien is het aantal speekselkliercarcinomen per hoofd-halscentrum dusdanig laag (soms 'slechts' 3 patiënten per jaar), dat er over kwaliteit van zorg geen statistisch valide uitspraken gedaan kunnen worden. Verdere centralisatie lijkt hiervoor een oplossing te kunnen bieden. Kanttekening daarbij is dat maligne speekselkliertumoren voorafgaand aan chirurgie niet altijd te onderscheiden zijn van benigne speekselkliertumoren.
De door de NWHHT geïnitieerde prospectieve landelijke registratie van alle hoofd-halstumoren in de 'Dutch Head and Neck Audit (DHNA)' zal ons meer gedetailleerde informatie verstrekken over de richtlijn adherentie, case-mix verschillen tussen de centra en eventuele verschillen in uitkomsten tussen de centra. Bovenal kan dit tot kritische introspectie leiden, waardoor potentiële verbeterpunten vroegtijdig gesignaleerd worden en als verbeterprojecten opgepakt kunnen worden. Essentiële voorwaarde voor het slagen van zo'n registratie is transparantie van de resultaten van de deelnemende centra.

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AUTHORS AND AFFILIATIONS

R.J. Baatenburg de Jong, MD, PhD.
Department of Head and Neck Surgery and Otorhinolaryngology, Erasmus Medical Center, Rotterdam, The Netherlands

A.J.M. Balm, MD, PhD.
Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands.
Department of Oral and Maxillofacial Surgery, Academic Medical Centre, Amsterdam, The Netherlands.

M.W. M. van den Brekel, MD, PhD.
Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands.
Department of Oral and Maxillofacial Surgery, Academic Medical Centre, Amsterdam, The Netherlands.
Institute of phonetic sciences, University of Amsterdam, Amsterdam, The Netherlands.

E.C. van den Broek, MD, PhD.
The nationwide network and registry of histo- and cytopathology in the Netherlands (PALGA), Houten, The Netherlands.

H. Bouman, MD, PhD.
Department of Head and Neck Surgery and Otorhinolaryngology, Rijnstate hospital, Department of otorhinolaryngology, Arnhem, the Netherlands

B.A.C. van Dijk, MD, PhD.
Department of Research, Comprehensive Cancer Organisation (IKNL) The Netherlands,
Utrecht, The Netherlands.
Department of Epidemiology, University of Groningen, University Medical Centre, Groningen, The Netherlands.

O. Hamming-Vrieze, MD.
Department of Radiation Oncology, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands

M.C. van Harten, MD.
Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands.

M. Hauptmann, MD, PhD.
Department of Epidemiology and Biostatistics, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands

I. Hegger.
Department of Pathology, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands

C.C.M. Marres, MD.
Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands.

A. Navran, MD.
Department of Radiation Oncology, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands

R.J.E. Sedee, MD.
Department of Head and Neck Surgery and Otorhinolaryngology, Medical Center Haaglanden, The Hague, The Netherlands

M. Slingerland , MD, PhD.
Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

L.E. Smeele, MD, PhD.
Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands.
Department of Oral and Maxillofacial Surgery, Academic Medical Centre, Amsterdam, The Netherlands.

M.M. Stuiver, MD, PhD.
Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands

R.J. Takes, MD, PhD.
Department of Head and Neck Surgery and Otorhinolaryngology, Radboud University Medical Center, Nijmegen, The Netherlands

C.H.J. Terhaard, MD, PhD.
Department of Radiation Oncology, University Medical Center Utrecht, Utrecht, The Netherlands

M.H. Valstar, MD.
Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute -Antoni van Leeuwenhoek, Amsterdam, The Netherlands.
Department of Oral and Maxillofacial Surgery, Academic Medical Centre, Amsterdam, The Netherlands.

M..L.F. van Velthuysen, MD, PhD.
Department of Pathology Erasmus Medical Centre, Rotterdam, The Netherlands.

J.G.A.M. de Visscher, MD, PhD.
Department of Oral and Maxillofacial Surgery, Medical Center Leeuwarden, Leeuwarden, The Netherlands

S.M. Willems, MD, PhD.
Department of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands
Department of Pathology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, The Netherlands.
The nationwide network and registry of histo- and cytopathology in the Netherlands (PALGA), Houten, The Netherlands.

M.W.J.M. Wouters, MD, PhD.
Department of Surgical Oncology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, The Netherlands.

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* Both authors contributed equally

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Curriculum vitae Auctoris

Mischa de Ridder is geboren op 26 februari 1986 te Woudenberg, waar hij ook opgroeide. Hij doorliep het Atheneum met de profielen natuur & gezondheid en natuur & techniek op het Ichthus college te Veenendaal. Daarna volgde hij de studie geneeskunde aan de Radboud Universiteit in Nijmegen. Tijdens de studie groeide de interesse voor de oncologische zorg wat er toe leidde dat hij een afsluitend coschap deed in het Antoni van Leeuwenhoek te Amsterdam op de afdeling hoofd-halsoncologie onder leiding van prof.dr. A.J.M. Balm. Direct na het behalen van zijn artsendiploma in december 2011 startte hij als arts-assistent voor de heelkundig oncologische disciplines in het Antoni van Leeuwenhoek onder leiding van dr. J.A van der Hage en dr. W.M.C. Klop. Dit combineerde hij met het promotie-onderzoek naar kwaliteitsindicatoren voor hoofd-halsoncologische zorg in Nederland onder leiding van prof.dr. A.J.M. Balm en prof.dr. L.E. Smeele.
In 2014 startte hij met de opleiding tot radiotherapeut-oncoloog in het Academisch Medisch Centrum Amsterdam onder leiding van prof.dr. L.J.A. Stalpers en prof.dr. C.R.N. Rasch.

Hij is getrouwd met Denise de Ridder en heeft drie kinderen Amé (2012), Loudi (2014) en Olav (2016).

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