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HTA-Report | Summary

The impact of microsurgery, stereotactic radiosurgery and radiotherapy in the treatment of meningiomas depending on different localizations

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Health political background

In the past, the objective of surgery was a complete resection of the tumor, resulting however in a high morbidity and in part strong neurological malfunctions. Nowadays this approach has changed. The surgical strategy takes the medical condition, localisation and extension of the meningioma much more into account and aims on preserving neurological functions, reducing symptoms and improving the overall medical condition. Correspondingly, the significance of the radiotherapeutical intervention increases, which is most common deployed as a complementary, especially in cases of tumor, residual or recurrence. Stereotactic radiosurgery (SRS) is a one of the non-invasive treatment techniques. The treatment with the Gamma Knife is already possible since 1986, but only due to recent advances in imaging techniques this technique gained importance. Currently, in Germany four centres exist which provide Gamma Knife therapy. SRS also can be realised by systems based on a linear accelerator (e. g. Cyberknife, Novalis). The high precision of the intervention is due to the low invasiveness of the treatment resulting in low injury of surrounding tissue. This is of high relevance as the minimisation of the invasiveness becomes increasingly important. SRS can be an outpatient treatment, which complies with the aims of health policy to shift health services from the inpatient to the outpatient health sector. Sophisticated technical equipment is needed in order to deploy SRS, which brings along high investment and operating costs. As SRS is classified as outpatient treatment, investment costs for the equipment are not covered according to the dual hospital finance system, thus, have to be covered by revenues from treatment of patients.
Accordingly, the question has to be answered, whether it is necessary to build a comprehensive network of SRS centers for all patients with a corresponding indication.

Scientific background

Meningiomas comprise nearly 20 % of all intracranial neoplasms and thus represent the most important group. In 85 % of all cases meningiomas are benign tumors. Consequently, the five year survival rate for meningioma patients amount to nearly 90 %. In most cases these tumors grow slowly and do not spread metastases. In the majority of the cases the tumor is well encapsulated against surrounding brain tissue and is well provided with blood. In most cases meningiomas grow into the meninx, less often they can be found destroying the overlying bone. As meningiomas arise from arachnoidal cap cells, meningiomas can be found in different localisations

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and can be associated with different symptoms as well as complaints. In most cases meningiomas can be found at the falx (separating cerebral membrane between the cerebral hemispheres), convexity and sphenoid wing. Meningiomas seldom are spinal neoplasms. The incidence of meningiomas in Germany is reported to be six of 100,000 persons. 2 % of meningiomas are diagnosed during childhood and adolescence, but in most cases the mean age of patients is in the mid forties.

The reason for emergence of meningiomas has not been identified completely so far. Some studies indicate that changes in the genetic makeup facilitate development. Meningiomas are usually diagnosed as a lesion expansion within the skullcap. Symptoms differ between localisation, size and dimensions of the tumor. For a long time these tumors are without any symptoms. Meningiomas are often diagnosed by chance. In that case the therapist may well suggest a wait-and-see strategy. In recent years the number of asymptomatic meningiomas has increased, while the number of symptomatic meningiomas (patients with discomforts or neurological deficits) remains constant.

The treatment strategy may vary depending on the tumor localisation and the pace of proliferation. If possible, a microsurgical removal of the tumor using a transcranium approach can be seen as first choice in therapy, as a complete healing is possible in the case of a complete removal of the tumor. With a microsurgical removal a volume reduction and a fast relief of strain on the surrounding tissue can be achieved immediately. Due to observations of patients with asymptomatic tumors, which were detected just by chance, just the observation of the tumor may also be chosen. This especially applies for tumors in close vicinity to sensible structures, where a complete removal by a surgical intervention is associated with a high risk of damaging these structures and thus exposing the patient to the risk of severe neuronal deficiencies and morbidity. In this case, non-invasive treatment techniques can be chosen to complement therapy. Conventional fractionated radiotherapy, stereotactic radiotherapy and SRS are methods of additional treatment.

Research questions

Medical question

Research questions identified to be tackled within this HTA-report are focused on treatment strategies of meningiomas and their outcome with respect to different localisations of the tumor. In this context the effects of the therapy on the health-related quality of life are considered as well. Thus the following research question is put from the medical point of view: What is the medical efficacy of SRS deployed for treating meningioma compared to a surgical treatment strategy, with or without adjuvant radiotherapy?

Health-economic question

Economic assessment focuses on the structure of costs of different treatment strategies. Accordingly, the following research question is put from the health-economic point of view: What are the costs of radiosurgery compared to the microsurgical treatment in the context of the German health care system?

Methods of literature selection

Systematic literature search

Systematic literature search is conducted in the most important medical electronic databases MEDLINE, EMBASE and Cochrane Library. Other integrated databases are the international databases for health technology assessment DAHTA, INAHTA and NHSEED. The comprehensive repertory of subjects searched includes terms from medicine, economics, ethics and law. Each step of the literature search is documented to assure reproducibility of the results obtained from literature search.

Inclusion criteria

Whilst taking account the research question, comparative and non comparative clinical studies for treatment strategies of meningiomas are included. Studies have to include at least retrospectively defined groups of patients. They have to provide an adequate description of the patient population and of the follow up. All studies are required to examine at least 20 patients and to realise a follow up time of at least 36 months.
The same inclusion criteria regarding size of treatment groups and evidence are relevant for publications selected to answer the health economic research question. These publications should provide results on the analysis of the costs of one ore more treatment techniques.

Exclusion criteria

Those publications are excluded for which no link to the defined research questions can be made and which for instance only cover general topics or descriptions of one ore more techniques. Case studies and unsystematic literature reviews, expert opinions, consensus papers and other unsystematic publications are excluded as well. If the follow up time and the number of patients do not match the inclusion criteria set, these studies are not included.

Data analysis

Medical evaluation

The medical evaluation starts with a description of the study deploying a standardised report form. This approach assures a standardisation in presenting the facts named in the evaluated study and supports the analysis and the presentation of weaknesses and unspecific statements.
The next step is to visualise the treatment procedures described and analysed in each publication via flow chart. In the case of surgical treatment approaches, the visualisation also takes into account the different locations of the tumor, as these have a significant impact on the therapeutical outcome. As for radiotherapeutic treatment approaches, this differentiation is not made due to the fact that studies with a radiotherapeutic focus do not differ between patients and results regarding the tumor localisation. The different states of health after treatment and their frequency of occurrence is visualised according to the numbers given in literature.

Health-economic evaluation

The standardised report form is also used for the evaluation of the literature on health-economic topics. The very small amount of literature covering health-economic aspects however makes the analysis very difficult. Neither

cost-utility analyses nor cost-benefit analysises can be identified with the literature search. In order to compensate this, the health-economic assessment is additionally based on data on costs from the InEK (the German DRG Institute). The structure of refunding is presented taking into account the German healthcare system.

Aspects found on ethics and law

No literature could be identified.

Results

Quantitative results

The literature search focusing on medical efficacy comes up with 2.167 publications. 167 of them are analysed as fulltext. Of these, 31 publications are selected via a multi-level selection procedure to answer the questions raised in this HTA-report. These comprise four publications, which focus on medical efficacy including the health-related quality of life.
The database research with a focus on health-economics, law and ethics results in 149 references. After the review of abstracts nine are included for full-text review. The additional internet and literature based hand search on law, ethics and economics yields six publications, which sums up to 15 publications for full-text review. Three publications are found to be suitable to answer the questions raised, two of them covering aspects of health-economics, one focusing on health-related quality of life.

Medical evaluation

The results presented in the literature published by surgeons strongly vary regarding the localisation of meningiomas. Detailed results can be taken from the different chapters of this assessment report.
Those publications not differentiating between the localisation of meningiomas name a progression free survival rate of five years in 77 to 97 % of the cases after complete surgical resection of the tumor, in 18 to 70 % of the cases after subtotal resection and for patients who had undergone surgical resection and a combined radiotherapeutical treatment of their meningiomas a five year progression free survival rate between 82 and 97 %. Other treatment options like hormone therapy or treatments to stop tumor growth had been used unsuccessfully so far.
A study with a larger group of 504 patients with WHO grade I meningiomas treated by microsurgery and 170 patients receiving radiotherapeutic treatment of grade I meningiomas shows the recurrence rate depends on the extent of resection achieved during the intervention. The recurrence rate of meningiomas of 16 and 20 % respectively was measured were a Simpson´s grade I or II could be achieved. In contrast, the recurrence rate reaches 70 % after interventions with Simpson´s grade IV resections. The progression free survival rate after three years and after seven years are 100 % and 96 % after Simpson´s grade I resection and 91 % and 92 % after Simpson´s grade II resection. If patients are treated with radiosurgery the progression free survival rate amounts 100 % and 96 % at follow up after three and seven years, respectively.

Economic evaluation

In the publications included in the assessment the costs associated with the delivery of radiosurgery in comparison to the costs associated with the delivery of microsurgical therapy are reported to be lower, between 27 % and 29 %. Accordingly, radiosurgery can be delivered less expensive. The costs for the delivery of radiosurgery however strongly depend on the number of patients treated, as investment and service costs have to be divided by the number of patients treated. It has to be noted that the present papers solely investigate the costs associated with the treatment delivery. Costs depending on the outcome of treatment are not taken into account.

Differences in status between different types of therapy can be found using the Karnofsky performance status scale. It was found that in the long run patients receiving radio- or microsurgery reach a Karnofsky performance status scale accounting for normal activity, with minor symptoms at most. Right after surgery, patients receiving microsurgery treatment however suffer from a short time decrease in performance status measured by the Karnofsky scale. These patients are unable to carry on normal activities and are not able to work. This decrease in performance status could not be observed in patients receiving radiosurgery treatment. As however the mean score of the preoperative Karnofsky performance status is different for both groups, the comparability of the results is questionable.

Discussion

In general, studies are initiated depending on the therapeutic approach, which shows regional differences to a large extend. Most patients are first introduced to surgeons, who suggest and realise a surgical therapy. Depending on collaborations and capabilities, the patient is afterwards offered a complementing radiotherapeutic treatment. The radiotherapist in these cases is faced with tumors of different sizes, resected to different extends and in parts located close to critical structures, which leaves not many choices for treatment. Accordingly, the design of many studies can be explained, resulting in non-systematic and non-randomised groups of patients, and only some studies clearly separate groups of patients by randomisation or with continuous follow up of different patient groups.

Different requirements and possibilities result in different criteria of decision. Furthermore, different indicators for assessment of the therapeutical outcome have been introduced. The result of surgical resection of tumors is quantified based on a scale introduced by Simpson in 1957, distinguishing four grades. These grades take into account the extent of the tumor and the dura resection. The assessment of the radiotherapeutical treatment outcome is described by the extent of the tumor volume control (in terms of volume reduction or stable volume), as well as in terms used in oncology, such as progression free survival and survival rate with respect to years lived. Which criteria and parameters are used to assess outcome differs between studies. Because of such large variance in assessment parameters, a comparison between studies is scarcely possible.

Conclusion

Due to the strong influence of the tumor localisation on the outcome of microsurgical treatment, of the publications presented a surgical therapy approach can be suggested only with respect to the tumor localisation. Taking into account this strong dependence on the tumor localisation, the outcomes of microsurgical treatment cannot be compared to outcomes presented in the publications focusing on radiotherapy, as the latter in general do not distinguish groups of patients regarding the tumor localisation. Thus, in most cases a decision on the right approach to treat has to be decided based on the medical condition of the patient, the experience of the treating physician, the capabilities for radiotherapy, and the personal preferences of the patient.

Only for patients with tumors with a spinal localisation or WHO Grade I meningiomas with a cortical localisation, a primary treatment by microsurgery can be suggested. For all other localisations of tumors, an alternative treatment by means of radiosurgery should be discussed. From the literature identified, a clear recommendation of one or the other therapy however can not be deduced. Patient management by the family physician, neurologist or neurosurgeon first consulted of the patient is an important factor. Patients seldom see a radiosurgeon first. Therefore a tendency for treatment is determined at that time.

Concerning treatment costs there is no data available specifically focusing on radiosurgical treatment of the meningiomas. In most cases patients with meningiomas are only one part of the population study. Thus there is a strong need for randomised clinical trials or prospective or contrasting cohort studies, which compare rigorously microsurgery with radiosurgery with respect to the different localisations of tumors.