IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Positron emission tomography (PET) and PET/CT for recurrence diagnosis in high-grade malignant glioma (grades III and IV)[1]

Executive Summary

[1] Translation of the executive summary of the final report "Positronenemissionstomographie (PET) und PET/CT zur Rezidivdiagnostik bei Gliomen mit hohem Malignitätsgrad (III und IV)" (Version 1.0; Status: 22.11.2010). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Background

Malignant glioma (grades III and IV according to the WHO) is one of the most malignant types of cancer. It may be accompanied by serious impairment of neurological functions and in most cases has a very poor prognosis. The reason for the development of glioma is still not fully clear. After diagnosis, surgical removal of the tumour is usually the therapy of first choice. High-grade glioma can seldom be fully removed by means of surgery. The goal of surgery is primarily to restrict the expansion of the tumour and the associated neurological symptoms. Surgical removal is supplemented by chemo- and/or radiation therapy.

First studies on PET in the diagnosis of brain tumours had already been published in the early 1980s. Through the use of PET in malignant glioma it is hoped to identify processes that evade detection by CT or MRT, to categorize detected tumours more reliably to the correct disease stage or determine their volume, and, in the case of justified suspicion, to diagnose (or exclude) tumour recurrence with greater certainty. Particularly in recurrence diagnosis it is crucial to make a more precise distinction between “real” recurrences and radiation necroses.

Research question

The present investigation followed 2 aims:

1 Determination of the patient-relevant benefit of PET and PET/CT

The primary aim of this report was to describe the patient-relevant benefit that doctors and patients can expect from imaging methods with PET and PET/CT in the recurrence diagnosis of highly malignant glioma. “Benefit” was understood here to mean changes that are causally attributed to the use of PET and have perceptible consequences for the patient.

2 Assessment of the diagnostic and prognostic accuracy of PET and PET/CT

If too few informative trials to determine the patient-relevant benefit (first goal) were identified, a systematic assessment of the diagnostic and prognostic accuracy of PET and PET/CT was also to be carried out (second goal). In this context it was to be examined to what extent PET and PET/CT are superior to standard diagnostic procedures without PET. In other words, does the use of PET and PET/CT improve the rate of correct diagnoses or of the correct exclusion of recurrences? Similarly, does the use of PET and PET/CT enable more reliable prognostic statements on the occurrence of a recurrence than is possible with existing standard diagnostic procedures?

Methods

(Randomized) controlled comparative trials (strategy with vs. without PET) with patient-relevant outcomes (e.g. reduced mortality/morbidity) were to be considered for the benefit assessment within the framework of a systematic review. Evidence syntheses or alternatively prospective cohort and cross-sectional studies were to be systematically searched for and summarized for the assessment of test accuracy.

A systematic literature search was performed in the following databases to identify primary studies: EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials (Clinical Trials). An additional search was performed in the following databases to identify evidence syntheses: the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment Database (HTA). In addition, the following sources were screened: documents submitted by the Federal Joint Committee, publicly available study registries, queries to authors, documents submitted within the framework of the hearing on the preliminary report plan and preliminary report, as well as databases of guideline developers. The period up to 5 July 2010 was covered. In addition, reference lists of potentially relevant evidence syntheses were scrutinized.

The literature screening was performed by 2 reviewers independently of each other. After an assessment of study quality, the results of the individual studies were organized and described according to the research questions. IQWiG's preliminary benefit assessment, the preliminary report, was published on the Internet, and interested persons and parties were invited to submit comments within the framework of a hearing.

Results

The systematic search for published literature did not result in any comparative primary study that would allow a statement on the patient-relevant (additional) benefit of PET in the detection of recurrence of malignant glioma. Likewise, no evidence synthesis of sufficient quality was identified that summarized the available studies on the diagnostic and prognostic accuracy of PET in malignant glioma. The second research question was therefore answered on the basis of primary literature.

Of 12 primary studies identified that fulfilled the inclusion criteria of this report, 11 showed a high risk of bias. The only study with a low risk of bias included data on merely 12 patients and achieved only true-positive results. Moreover, the studies were published over a period of 21 years, which is inevitably associated with great heterogeneity of device quality and of clinical experience in the indication investigated.

The point estimates varied considerably for sensitivity and specificity of PET and the fusioned procedure (PET/MRT), whereby it was unclear whether this was due to the low number of patients included, the different tracers, the cut-off values defined for positive PET results, the reference tests used or the high risk of bias of the studies included. For these reasons, no reliable statements are possible, neither on diagnostic accuracy nor on the prognostic value of PET in the detection of recurrence of malignant glioma. Comparisons between different types of PET (tracers, integrated devices versus single devices, etc.) or between PET and other imaging methods cannot be inferred from the studies included.

None of the studies included reported what consequences the change in diagnostic procedure had on the management of the patients investigated.

Conclusions

The benefit of PET and PET/CT in the detection of recurrence of malignant glioma has not been proven.

Few studies exist so far on the diagnostic and prognostic accuracy of PET and PET/CT in this indication. The 12 primary studies included in this report are all very small (small precision) and, except for one, show methodological deficiencies (high risk of bias of results). In addition, the patient groups investigated, the tracers used, the threshold values and reference tests differ so considerably that no summarizing statements or comparisons of the different types of PET diagnostic procedures (devices, tracers, etc.) are possible.

Further studies are urgently needed to reliably assess the diagnostic and prognostic accuracy and in particular the patient-relevant benefit or harm of PET and PET/CT in the detection of recurrence of malignant glioma. Due to the low number of cases and the very poor prognosis in many patients with malignant glioma, multi-centre studies are needed – ideally involving international cooperation – and in particular studies of high-quality methodological design, in order to obtain robust data within a reasonable period of time.

Keywords: positron emission tomography, computer tomography, glioma, recurrence, treatment residuals, systematic review

The full report (in German) is available on www.iqwig.de