IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Positron emission tomography (PET) and PET/CT in bone and soft tissue tumours[1]

Executive Summary

[1] Translation of the executive summary of the final report "Positronenemissionstomographie (PET) und PET/CT bei Knochen- und Weichteiltumoren" (Version 1.0; Status: 20.12.2012). 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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This report was prepared in collaboration with external experts. According to § 139b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose "all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received." The Institute received the completed form "Disclosure of conflicts of interest" from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts and external reviewers is presented in Appendix F of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

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IQWiG thanks the external reviewer for his comments on the preliminary report. However, the external reviewer was not involved in the preparation of the final report. Individual sections and conclusions in the final report therefore do not necessarily reflect his opinion.

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[2] Due to legal data protection regulations, employees have the right not to be named.

Background

On 21.12.2006, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to search for, present and assess current medical knowledge about positron emission tomography (PET), and the integrated use of PET and computed tomography (PET/CT), in 14 different diseases. This final report concerns the part of the commission regarding bone and soft tissue tumours.

Research question

The present report had 2 goals:

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

The primary goal of the report was to describe the patient-relevant benefit that doctors and patients can expect from the imaging techniques PET and PET/CT in the primary diagnostics, primary staging, restaging and recurrence diagnostics of bone and soft tissue tumours. "Benefit" was understood here to mean the changes that are causally attributed to the use of PET or PET/CT and that have perceptible consequences for the patient.

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

If too few informative studies to determine the patient-relevant benefit were identified (first goal), 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, the extent to which PET and PET/CT are superior to standard diagnostic techniques without PET was to be examined. In other words, does the use of PET or PET/CT improve primary diagnostics, primary staging, restaging, or the correct exclusion of recurrences? It was also to be tested whether, by means of PET or PET/CT, more reliable prognostic conclusions can be drawn within the framework of the indications mentioned than is possible with current standard diagnostic techniques.

Methods

(Randomized) controlled trials (RCTs) – e.g. strategy with versus without PET or PET/CT – with patient-relevant outcomes (e.g. reduced mortality/morbidity) were to be considered for the benefit assessment within the framework of a systematic review.

Diagnostic and prognostic accuracy were to be evaluated by a "Review of Reviews", i.e. an assessment based on published evidence syntheses. For the time period and research questions not covered by its literature search for the most recent evidence synthesis, the Institute was to conduct supplementary searches to identify additionally relevant primary literature (prospective cohort and cross-sectional studies).

Within the framework of the supplementary search, a systematic literature search for studies on diagnostic and prognostic accuracy was conducted in the following databases: EMBASE, MEDLINE and the Cochrane Central Register of Controlled Trials (Clinical Trials). In addition, the following databases were screened to identify evidence syntheses: the Cochrane

Database of Systematic Reviews (Cochrane Reviews), the Database of Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). The last search was conducted on 24.05.2012.

In addition, potentially relevant evidence syntheses, publicly accessible trial registries and conference proceedings were searched, as were documents submitted by the G-BA and publications submitted within the framework of the hearing on the preliminary report plan and on the preliminary report. Moreover, requests were sent to authors of relevant published studies to clarify key questions.

The literature screening was conducted by 2 reviewers independently of each other. After an assessment of study quality, the results of the individual studies were organized according to research questions and described. In addition, studies included within the framework of the supplementary search were assessed with regard to their transferability to the German health care context.

Results

Patient-relevant benefit

The systematic search for published literature did not identify any comparative study that would allow a conclusion to be drawn on the patient-relevant (added) benefit of PET and PET/CT in bone and soft tissue tumours. Likewise, the search in trial registries and conference proceedings did not identify any ongoing comparative studies on this disease.

Diagnostic and prognostic accuracy

No evidence synthesis that fulfilled the inclusion criteria of this report was found on the diagnostic and prognostic accuracy of PET for any of the 4 indications. Diagnostic and prognostic accuracy of PET were therefore assessed exclusively on the basis of primary studies.

32 primary studies (39 publications) fulfilled the inclusion criteria of this report (primary diagnostics [n = 12], primary staging [n = 3, 2 of which were prognostic studies], restaging [n = 13, 3 of which were prognostic studies; one study provided both diagnostic and prognostic data], recurrence detection [n = 1], spanning several indications [n = 5]; 2 studies provided data on 2 indications).

In all indications, with the exception of restaging, almost all primary studies reported data on the diagnostic accuracy of PET; only one study reported data on the diagnostic accuracy of PET/CT. In the indication “restaging”, however, most (7 of 11) primary studies reported data on the diagnostic accuracy of PET/CT. All diagnostic PET and PET/CT studies used the tracer FDG. Additional tracers (FLT, [^{11}C]-choline, FES) were used in 3 studies. The tracer FDG was used in 3 of the 4 prognostic studies, and the tracer [^{11}C]-methionine was used in the fourth one. Seven studies were assessed as having a low risk of bias, 24 studies were

assessed as having a high risk of bias, and one study was assessed as having a high risk of bias regarding one analysis, and a low risk of bias regarding the other analysis.

Direct comparisons between PET or PET/CT and other diagnostic techniques were reported in 8 of the 32 primary studies (Strobel 2008, Yoshida 2008, Völker 2007, Bajpai 2011, Cheon 2009, Im 2012, Denecke 2010, and Benz 2009; see Table 56 of the full report). Exclusively data on diagnostic accuracy were reported in all 8 studies with direct comparisons. There were no studies with direct comparisons on prognostic accuracy. None of the 8 studies reported a statistically significantly higher diagnostic accuracy of PET or PET/CT versus a comparator technology; however, a statistical analysis was only reported in 2 of the 8 studies. The results of all 8 studies are subject to great uncertainty because of the small number of patients and the high risk of bias. Bivariate meta-analyses were not possible in any of the 4 indications because the 8 studies with direct comparisons differed in the examined indications, patient populations, and/or comparator technologies.

Conclusions

With regard to the first question of the report, the patient-relevant benefit, no results of completed studies could be identified. Therefore, the patient-relevant benefit of PET and PET/CT in bone and soft tissue tumours could not be assessed or proven.

Regarding the second question of the report, the diagnostic and prognostic accuracy, a total of 32 primary studies (39 publications) could be included. Direct comparisons between PET or PET/CT and other diagnostic techniques were described in 8 of the 32 primary studies on diagnostic accuracy, and in no study on prognostic accuracy. None of the 8 studies reported a statistically significantly higher diagnostic accuracy of PET or PET/CT versus a comparator technology. In addition, bivariate meta-analyses were not possible in any of the 4 indications. Therefore, no definite conclusions can be drawn on a possible superiority of PET or PET/CT versus other diagnostic techniques, neither for diagnostic nor prognostic accuracy.

Studies of reliable methodology are urgently required to be able to assess the patient-relevant benefit or harm of PET and PET/CT in bone and soft tissue tumours. An ongoing multinational study on Ewing sarcoma (EWING 2008) might be able to deliver informative results on the role of PET and PET/CT when choosing optimum therapy. No other ongoing studies could be identified.

Keywords: positron-emission tomography, tomography, X-ray computed, soft tissue neoplasms, bone neoplasms diagnosis, staging, recurrence, systematic review

The full report (German version) is published under www.iqwig.de.