IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Positron emission tomography (PET) and PET/CT in oesophageal cancer[1]

Executive Summary

[1] Translation of the executive summary of the final report "Positronenemissionstomographie (PET) und PET/CT bei Ösophaguskarzinom" (Version 1.0; Status: 24 June 2013). 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. The preliminary report underwent an external review.

IQWiG is solely responsible for the content of the report.

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

Executive summary

With its letter of 21 December 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), including the integrated use of PET and computed tomography (PET/CT), in 14 different diseases. This final report concerns the part of the commission regarding oesophageal cancer.

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 PET and PET/CT in the primary staging, restaging and recurrence diagnostics of oesophageal cancer. "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), an 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 staging, restaging, or the detection 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. a 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 the literature search of the most recent evidence synthesis, IQWiG was to conduct a supplementary search to identify additional relevant primary literature (prospective cohort and cross-sectional studies).

A systematic literature search for RCTs (within the framework of the benefit assessment) and for studies on diagnostic and prognostic accuracy (within the framework of the supplementary search) 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 18 May 2012.

Moreover, the following sources were also searched: documents submitted by the G-BA, publicly accessible trial registries, documents submitted in the hearing on the preliminary report plan, databases of developers of clinical practice guidelines, 4 conference proceedings, as well as the reference lists of potentially relevant evidence syntheses.

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 for any research question of the present report that would allow conclusions to be drawn on the patient-relevant (added) benefit of PET and PET/CT for the questions concerning primary staging, restaging and recurrence diagnostics. Likewise, the search in conference proceedings identified no references to ongoing comparative studies. Four ongoing studies were identified in trial registries.

Diagnostic and prognostic accuracy

Three evidence syntheses and 37 primary studies from the supplementary search fulfilled the inclusion criteria of this report. Eleven primary studies from the evidence syntheses, which solely investigated the indication “restaging”, fulfilled the inclusion criteria of this report. Therefore this report is based on a total of 48 primary studies: primary staging (n = 25), restaging (n = 19) and recurrence diagnostics (n = 4).

Primary staging

For N-staging, direct comparisons between PET and CT were investigated in 12 studies. No statistically significant difference between the diagnostic accuracy of PET and CT could be determined in the bivariate meta-analyses for N-staging.

For M-staging, direct comparisons between PET and CT were investigated in 7 studies. The results of this meta-analysis were not presented, as the data in these 7 studies were not suited to calculated precise estimates, nor did the sensitivity analyses produce precise estimates.

In 1 prognostic study a direct comparison of FDG-PET and TI-SPECT was performed. None of the characteristics relevant to PET and SPECT showed a statistically significant connection after multifactorial modelling.

Restaging

Direct comparisons for restaging after completion of neoadjuvant therapy were performed in 3 studies:

The comparison PET/CT versus endosonography (EUS) was investigated in the study by Cerfolio 2005. For PET/CT a sensitivity of 86.7% (95% CI [59.7; 98.3]) and a specificity of 87.9% (95% CI [71.8; 96.6]) were shown. In contrast, EUS showed a sensitivity of 20% (95% CI [4; 48]) and a specificity of 94% (95% CI [79.8; 99.3]). PET versus PET/CT was investigated in the study by Roedl 2009. A sensitivity of 59% (95% CI [36.4; 79.3]) and a specificity of 100% (95% CI [87.2; 100]) were shown here for PET. PET/CT achieved a sensitivity of 68% (95% CI [45.1; 86.1]) and a specificity of 100% (95% CI [87.2; 100]). PET was compared with EUS and CT on the basis of 10 and 11 included patients in the study by Kroep 2003. A sensitivity of 100% (95% CI [39.8; 100]) and a specificity of 100% (95% CI [54.1; 100]) were shown for PET. The comparator technology EUS also showed a sensitivity of 100% (95% CI [47.8; 100]) and a specificity of 100% (95% CI [54.1; 100]). In contrast, CT showed a sensitivity of 50% (95% CI [6.8; 93.2]) and a specificity of 71% (95% CI [29.0; 96.3]).

Interim staging

One direct comparison of diagnostic technologies was available for interim staging:

In the study by Kroep 2003, PET was compared with EUS and CT on the basis of 11 included patients. PET showed a sensitivity of 100% (95% CI [39.8; 100]) and a specificity of 85.7% (95% CI [42.1; 99.6]). The comparator technology EUS showed a sensitivity of 100% (95% CI [47.8; 100]) and a specificity of 100% (95% CI [54.1; 100]). In contrast, CT showed a sensitivity of 50% (95% CI [6.8; 93.2]) and a specificity of 71% (95% CI [29.0; 96.3]).

As only 1 study was available for the indication “interim staging during neoadjuvant chemotherapy or chemoradiotherapy”, which investigated a direct comparison on the basis of only 11 patients, the results of the non-comparative study are also presented here as supplementary information. In the 7 studies the point estimates for the sensitivity of PET or PET/CT were in the range of 44% (corresponding specificity 52%) to 88.9% (corresponding specificity 61.4%). The point estimates for the specificity lay in the range of 52% (corresponding sensitivity 44%) to 78% (corresponding sensitivity 80%). Wide confidence intervals were observed for all point estimates.

Recurrence diagnostics

Four primary studies were included in the supplementary search. All 4 studies investigated the diagnostic accuracy of PET and PET/CT. One study additionally investigated prognostic accuracy.

No results were available for the direct comparison between PET or PET/CT and conventional diagnostics.

Conclusion

The patient-relevant benefit of PET or PET/CT in oesophageal cancer is not proven. Neither ongoing nor completed comparative intervention studies on the patient-relevant benefit of PET or PET/CT in oesophageal cancer were identified. Whether the use of PET or PET/CT also leads to an improvement in patient-relevant outcomes has not been investigated in any of the 3 indications.

For the second research question of the report, diagnostic and prognostic accuracy, a total of 48 primary studies were included from the 3 evidence syntheses considered and the supplementary search. Across all indications, a direct comparison of PET or PET/CT with other imaging techniques was performed in 19 studies. In 1 study the tracer FDG was compared directly with the tracer ^{11}C-choline.

Most studies were conducted in the indication "primary staging". 12 studies directly compared PET with CT in N-staging and 7 studies investigated the direct comparison of PET with CT in M-staging. For N-staging, no statistically significant difference between the diagnostic accuracy of PET and CT could be identified in the bivariate meta-analysis. For M-staging, the bivariate meta-analysis produced no precise estimates, so that no conclusions about the diagnostic accuracy of PET and CT can be drawn here either. Too few high-quality studies are available for the indications "restaging" and "recurrence diagnostics" to enable reliable conclusions on the diagnostic and prognostic accuracy of PET or PET/CT. In particular the advantage of this metabolic technique versus morphologic imaging techniques is unclear. To date, no completed parallel comparative studies on the patient-relevant benefit of PET or PET/CT in oesophageal cancer could be identified. Studies of high methodological quality are urgently needed (especially regarding the question of treatment response to neoadjuvant therapies) to enable the reliable assessment of the patient-relevant benefit or harm of PET or PET/CT in oesophageal cancer.

Keywords: positron-emission tomography, tomography, – X-ray computed, esophageal neoplasms, staging, recurrence, systematic review

The full report (German version) is published under https://www.iqwig.de/de/projekte_ergebnisse/projekte/nichtmedikamentoese_verfahren/d06_01h_positronen_emissions_tomographie_pet_bei_oesophaguskarzinom.1163.html.