

HTA-Report | Summary

Evaluation of optical coherence tomography in the diagnosis of age related macular degeneration compared with fluorescence angiography Stürzlinger H, Fröschl B, Genser D

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Health political background

Age-related macular degeneration (AMD) is a disease of the retina which can lead to blurred vision of the central part of the visual field and finally to central vision loss. Worldwide 25 to 30 million people suffer from AMD. In industrialised nations AMD is the most common cause of blindness and severe visual impairment.

Early detection plays a special role with regard to the more aggressive wet (or exsudative) form of AMD because here there are several therapies preventing further vision loss. For the final diagnosis of AMD two main methods are used: fluorescein angiography (FA; which is the gold standard) and optical coherence tomography (OCT). The FA is only reimbursed if there are concrete suspicious facts (like increased intra ocular pressure). OCT currently is not reimbursed in the ambulatory sector by compulsory health insurance.

Scientific background

AMD is a disease of the retina characterized by the accumulation of metabolic products in the macula, the part of the retina which is most important for central vision. The deposits are located in the inner part of the Bruch's membrane at the base of the retinal pigment epithelial cells. Drusen and pigment disorders occur in early stages. These changes are usually not associated with vision disorders. In late stages a dry form with slowly progressing atrophy of the retinal pigment epithelium (geographic atrophy) is distinguished from the exsudative form with choroidal neovascularisation, retinal pigment epithelial detachment and tears, which finally leads to scars of the retina. Growth factors such as "vascular endothelium growth factor" (VEGF) are involved in the pathogenesis of neovascularisation. The course of visual changes in patients with the dry form is often slow, whereas the wet form may be associated with a more rapid loss of vision. Since the central vision is affected, advanced stages of the wet form may lead to difficulties of daily life activities such as reading, driving and recognition of faces. Blindness due to AMD occurs rarely before the age of 70 and is most frequent above the age of 80.

Age and a positive family history for AMD are well known risk factors for AMD. The impact of genetic factors has been established in recent years. Smoking is the most important life style factor/environmental factor increasing the risk of AMD.

Anamnestic data, visual acuity, slit lamp examination and a binocular evaluation of the macula are recommended for diagnostic evaluation of AMD. The Amsler grid can be used for screening purposes and early diagnosis. FA is the gold standard for the diagnosis of AMD. A fluorescent dye has to be applied intravenously and its distribution is monitored in the blood vessels of the eye. This investigation is essential for the exact classification of DAHTA @DIMDI Waisenhausgasse 36-38a D-50676 Köln

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Within the scope of the



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the exsudative forms of AMD (classical, occult). The invasive character and possible allergic reactions are major disadvantages of this investigation. OCT is a more recent non-invasive imaging technique, which is easy to perform and free of risks. Interference patterns produced by low coherence light (wavelength 820 nm) are reflected from retinal tissues and a two-dimensional image of the retina can be produced.

Therapeutic options are limited for the treatment of the early stages of AMD, whereas several therapies are available for the exsudative form, such as laser photocoagulation and photodynamic therapy. New treatments of AMD include medications which block angiogenesis: steroids or antibodies such as anecortave acetate, triamcinolone acetonide, pegaptanib, ranibizumab or bevacizumab. Several questions including dosage, mode of application and duration of the therapy as well as long-term safety are being addressed in ongoing studies. Efficacy and efficiency of the therapy can depend on the subtype and stage of AMD. Therefore an exact diagnosis is essential.

Research questions

The aim of this HTA report is to investigate the efficacy as well as (economic) efficiency of OCT compared to FA. Moreover relevant ethical, societal and legal aspects are identified.

Methods

A systematic literature search was performed in 34 international databases which yielded 2324 articles. Following a two-part selection process according to predefined selection criteria only eight medical publications remained for inclusion for assessment. 99 articles were included as background literature wherein 15 publications were added by handsearch. Relevant legal acts regarding juridical aspects were searched. Information extraction and assessment of the eight included studies were performed according to predefined criteria.

Results

According to the selection criteria eight publications comparing OCT results with fluorescenceangiographic results in patients with AMD were identified for medical assessment. Both, the patients evaluated as well as the aims of the studies, are quite heterogenous. In most of the articles very selected patient groups are studied. According to the defined criteria the quality of the studies is low except for one study. The number of investigated patients is below 35 in four publications, between 35 and 61 in three studies, and above 100 in only one publication.

In one study 26 patients (36 eyes) with drusen were investigated. In the majority of the cases drusen could not be detected by OCT. These cases include small hard drusen, extrafoveal serous drusen or very small soft drusen. In another publication of the same group of authors less than half of the patients with geographic atrophy (37 patients, 55 eyes) can be diagnosed reliably. However, in one case an angiographically suspected choroidal neovascularisation could be confirmed by OCT. In addition, certain changes can by shown by OCT, which are not documented by FA, such as cystoid maculopathia and macular holes.

In another study OCT identified a retinal pigment epithelial detachment in all 16 patients with retinal pigment epithelial tears and in 14 of these patients one or more focal interruptions of the retinal pigment epithel were detected. One study investigates patients with choroidal neovascularization, 13 of



which are diagnosed as AMD. Neither by FA nor by OCT the boundary of the lesions could be determined in all cases, but OCT adds relevant information to the angiographic diagnosis.

The prevalence of cystoid macular edema was determined in 61 patients with subfoveal neovascular AMD. The results show that the OCT is a useful test to detect the presence of cystoid macular edema because the latter may be difficult to identify by FA.

OCT findings are correlated with angiographic signs of choroidal neovascularisation in retinal pigment epithelial detachment associated with AMD in 35 patients. In patients with choroidal neovascularisation at the margin of the pigment epithelial detachment the correlations between OCT and FA are better than in patients with choroidal neovascularisation beneath the detached retinal pigment epithelium.

The study with the highest quality evaluates the diagnostic accuracy of OCT compared to FA in 131 eyes of 118 patients suspected of having choroidal neovascularisation. For OCT the sensitivity for detecting new potentially treatable lesions (84 eyes with classic or occult choroidal neovascularisation or serous pigment epithelial detachment) is 96 % and the specificity is 66 %. Including stereo colour images leads to a sensitivity of 94 % and a specificity of 89 %.

Economic studies concerning the efficiency of OCT compared to FA could not be identified according to the pre-defined inclusion criteria. Two studies investigate AMD screening procedures (dilated funduscopic examination for identifying the number of people with early AMD and self-screening using the Amsler grid and ophthalmologic examination plus FA in case of positive screen results respectively). The results cannot be compared directly as the two analyses investigate different therapies and target populations as well as different alternatives and screening methods. Both show that AMD screening may be cost effective for an appropriate target population. However, no conclusions can be drawn with respect to how results might change because of a higher diagnostic accuracy (through the use of OCT). Additionally we investigated the costs of performing OCT and FA in the German ambulant sector from the perspective of either compulsory health insurance or the patient. Only cost ranges can be identified. For performing OCT – which is not paid for by social insurance – patients on average have to pay more than they (would) have to pay for FA.

Discussion

The number of studies investigating OCT compared to FA in patients with AMD is presently very limited and the quality of the studies is generally low. The patient groups investigated and the objectives of the studies are very heterogenous. The investigated patients with AMD are highly selected and the number of the investigated patients is usually low.

In spite of the above mentioned limitations all publications show uniformly and convincingly that OCT cannot yet replace FA. However, it has to be considered, that in the studies published so far older models of OCT have been used. Using newer models might change the findings for some classes or stages of AMD. In the study with the highest quality and the highest number of investigated patients the most recent type of OCT (OCT 3) was used. This study shows a high sensitivity of OCT for detecting treatable lesions of AMD, and therefore OCT has been recommended for the screening of new potentially treatable neovascularisations prior to the use of the more timeconsuming FA. Moreover, OCT yields additional diagnostic findings and may verify unclear findings of the FA. Therefore the application of OCT in addition to FA seems to be useful in several cases.



With regard to an economic assessment no concrete conclusions can be drawn as no economic evaluation covering the efficiency of OCT compared to FA could be identified. Before an economic model calculation can be done further clinical results are necessary as to how and for which patients exactly OCT may contribute to increasing diagnostic accuracy and influence the therapy decision. It may be that higher procedure costs when using OCT are offset by a more effective use of therapy options.

Conclusions / Recommendations

The studies evaluated in this report show that OCT yields diagnostic findings in addition to FA results. Unclear findings of FA can be clarified and in certain cases OCT can possibly replace FA. However, OCT cannot replace the gold standard FA during the primary diagnostic procedure.

Future studies have to show whether OCT may give diagnostic information essential for therapeutic decisions in addition to FA and whether it can replace FA in selected cases. The number of patients included in these studies should be high enough to answer relevant questions with sufficient statistical power. In particular for the control of therapeutic interventions (not a topic in this report) OCT could have some benefits compared to FA because it is not invasive, has a lower risk for adverse events and possibly also a better compliance.

No recommendation can be made at present from the economic point of view, as no economic assessments currently are available. Moreover, further clinical results as mentioned above should be gained first. An economic model calculation can be built upon the resulting findings.