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Editorial

Is salivary gland ultrasonography a useful tool in Sjögren's syndrome?

Are we ready to use it for bedside diagnosis?

This editorial refers to Is salivary gland ultrasonography a useful tool in Sjögren's syndrome? A systematic review, by Sandrine Jousse Joulin *et al*., doi: 10.1093/rheumatology/kev385, pages 789–800.

Jousse-Joulin *et al*. [1] have performed a literature review of major salivary gland (SG) ultrasonography (US) in Sjögren's syndrome (SS) patients. They reviewed Pubmed and Embase for publications from 1988 to 2013 that fulfilled the OMERACT criteria (truth, discrimination, feasibility). This study extends a recent study by Delli *et al.* [2] about diagnostic properties of US of the major salivary glands. This editorial highlights the pitfalls in using SGUS for diagnosis and points out that the method is not yet ready for bedside diagnosis by the practicing rheumatologist.

This excellent review is a key initial step in establishing guidelines for obtaining and analysing SGUS data. It also instructs general rheumatologists to use caution before applying SGUS to diagnose SS or evaluate therapy until they have undergone extensive training and perhaps certified in its use [3].

Of the 165 publications identified, only 31 met OMERACT criteria [1]. The sensitivity ranged from 46 to 91%, and the specificity from 73 to 98%. There was heterogeneity in the definition of US in B mode and a few studies that used US in colour mode.

The authors [1] concluded that SGUS is a valuable tool to detect salivary gland abnormalities in primary Sjögren's syndrome (pSS). However, there is considerable variation in the definition of US abnormalities. The authors have used an algorithm called QUADAS-2, a systematic approach for quality assessment of published articles about new diagnostic methods [4]. The studies that fulfilled the criteria used one or two trained expert ultrasonographers (at most) at the participating institution.

This comprehensive review in this article [1] by experts in salivary gland US and SS extends the previous publications by these authors in recent years. This critical literature review is the starting point by the working group for standardization of SGUS methodology in SS.

In the review by Jousse-Joulin *et al.* [1], several US brands were used and the electronic frequency of the probe varied from 5 to 15 MHz. However, precise guidelines to position the probe and details of image acquisition were rarely available even in the 31 selected publications.

Most articles assessed the four major salivary glands (two parotids and two submandibular glands) [1]. The scoring systems in the papers chosen for inclusion in this manuscript demonstrated great variability, but most used a semiquantitative scale, such as the original scoring system from De Vita *et al.* [5] or a later revision by Salaffi *et al.* [6]. The echogenicity of the gland was generally compared with the masseter muscle in B mode.

Among the papers chosen for study by the authors, six different scoring systems were used, and the authors of the 31 studies chosen for analysis frequently modified these [1]. The initial scoring systems used prior to 2005 evaluated parenchymal inhomogeneity on a scale from 0 (normal) to 3 (grossly abnormal) [5]. Later studies used a scoring system that was a composite of five components (each graded 0–3) including homogeneity, hypoechoic areas, hyperopic reflections, clearness of borders of the gland and presence of echogenicity (0 or 1).

Other studies developed their own scoring systems, which made comparison with other studies difficult. To overcome this problem, the EULAR formed a study group for SGUS standardization [7, 8] and this publication is an initial step in the process of establishing uniform criteria.

When used carefully by experienced US experts, US serves as an early tool for diagnosis of SS. However, US cannot be used as the sole diagnostic tool according to Cornec *et al*. [9]. The minor salivary gland biopsy remains the gold standard for diagnosis and with an US you can examine the major salivary glands. Further, histological features on minor SG biopsy such as germinal centre formation may provide prognostic information that is not available by SGUS.

Recent studies on a small number of minor salivary gland and parotid biopsies have shown a good correlation of changes in both sites [10]. However, comparison of US and pathology of a large number of parotid gland biopsies has not yet been reported. Thus, we still do not have the clinical–pathological correlation that will give us a basis for a SGUS classification system.

What is the lesson learned from this article [1] for the rheumatologist in the USA, where the practicing rheumatologist is now purchasing US equipment to use at the bedside? The key point is caution when diagnosing SS in the office with this new technique.

This article points out that among 161 publications from experts in the field of SS and ultrasonography, only 31 papers made the cut. Even then, the methodology of acquiring data and analysing data showed an unacceptable variability. A primary care physician or gynaecologist would not consider himself or herself competent to

evaluate (or biopsy) a nodule seen on US of breast, while the obstetrician routinely shows ultrasound scans to proud parents (and grandparents).

Although US is an upcoming modality in rheumatology and has been useful in evaluating joints, it is not yet ready for the practicing bedside rheumatologist to make diagnostic or therapeutic decisions regarding salivary glands. It should be considered a research tool until the operator has demonstrated competence and is perhaps certified to use this technically challenging method.

The reason for this stringent recommendation is that rheumatologists must consider the impact of an overread SGUS on patient anxiety and perhaps unnecessary treatment if an erroneous diagnosis of SS is made. The authors extend their recent publication [2] that suggests that stringent guidelines be followed to ensure high diagnostic quality in terms of sensitivity and specificity.

In summary, SGUS will play an important future role in improved diagnosis and monitoring of SS. This literature review article [1] is an important step to a uniform set of guidelines for obtaining and analysing SGUS.

For the practicing rheumatologist, more precise operator training is required to improve reproducibility and decrease intra-observer variation in SGUS [9]. The literature review and evidence grading by OMERACT methods in this article show that even US experts have high intra- and inter-observer error and no clear uniformly accepted methods exist for data analysis.

It is absolutely critical in clinical practice to recognize that a completely normal US scan provides helpful data (interpretable in the broader context) and a clearly abnormal US scan likewise similarly provides important data. However, a considerable number of US scans are reported as showing mild changes compatible with SS. Some of the published studies recognize this in their scoring systems with a cut-off for positivity above specific level but that level has not yet been universally accepted. This paper [1] is a first step in setting up an OMERACT standard that will allow us to move forward.

Thus, SGUS is not yet ready for the general rheumatologist to diagnose or treat at the bedside. The premature introduction of this promising method into general rheumatology practice by amateurs may actually harm our patients with misleading information, and impede the introduction of this promising diagnostic tool for diagnosis and monitoring therapy by expert ultrasonographers.

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