Interventional ultrasound: a critical overview on ultrasound-guided injections and biopsies

O. Epis, E. Bruschi

Rheumatology Unit, Niguarda "Ca' Granda" Hospital, Milan, Italy.

Oscar Epis, MD
Eleonora Bruschi, MD

Please address correspondence to:
Oscar Epis, MD,
Rheumatology Unit,
Niguarda Ca' Granda Hospital,
Piazza Ospedale Maggiore 3,
20162 Milan, Italy.
E-mail: oscar.epis@ospedaleniguarda.it

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ABSTRACT

Over the last decades ultrasound-guided procedures have become increasingly diffused in rheumatology, mainly thanks to the technical advances achieved in the ultrasound (US) field, combined with the greater availability, good portability and reduced cost of US devices, compared to other imaging techniques already used in rheumatology units. The direct visualisation of the tissue under analysis and the real-time imaging performance enabled by US-guidance account for an improved accuracy and directness in needle placement in a number of rheumatology interventions such as tendon and intra-articular injections. Compared with blind procedures, US-guided injections are more accurate and safe and they result in better clinical outcome in terms of joints improvement in function and decreased risk of damages caused by needle misplacement. The accuracy in needle placement of US-guided injections has proven to be important not only in common intra-articular injections, but especially in case of complex anatomical areas like the hip, facet and atlanto-occipital joints, where blinded injections are deemed poorly accurate and thus highly risky. Moreover US guidance can be successfully employed in more complex procedures such as synovial biopsy, portal establishment or arthroscopy, where US can also be combined with other imaging techniques.

Overall the employment of US-guided procedures is considered to be safe and well-tolerated, and increases the accuracy and therapeutic effectiveness of the interventions performed. This may pave the way for a more widespread employment of US-guidance in rheumatology units, and new studies could further explore the therapeutic advantages of these procedures.

Introduction

Over the last decades the use of ultrasound (US) has become widely spread in rheumatology, not only in terms of diagnosis and prognosis, but also as guidance in interventional procedures in place of other imaging techniques such as fluoroscopy, magnetic resonance imaging (MRI) or computed tomography (CT) (1, 2). The rapid diffusion of this technique is partially due to the technical advances in ultrasonography, which have led to performance improvements of the grey-scale ultrasound and to the development of more advanced forms of US such as 3D or Doppler US (1). In addition, US devices have become more easily available in rheumatology units, thanks to their good portability and the fact they are cheaper than MRI or CT devices (3). The number of US-guided interventions performed by rheumatologists has consequentially increased in the last decades, together with the number of ultrasonographers' training practices, given the specific expertise and skills required to perform this type of procedures (4). The increasing acceptance of US-guided procedures in clinical practice is also attested by the number of published papers on the subject: from 1980 to 2000 less than 1000 papers on US-guided injections or biopsies were published, while in the following decades (2001–2011) the same topic was covered by over 2500 publications (1). The improvements in image quality and accuracy have expanded the possibilities of US in interventional procedures such as biopsies or intra-articular administration of anti-inflammatory drugs, which require accurate needle placement. US-guided procedures enable not only a direct visualisation of the tissue under analysis but also, thanks to the real-time imaging performance, a continuous monitoring of the needle tip, together with a dynamic assess-

ment of joints and tendons movements and the possibility to detect unexpected structural abnormalities during the intervention. These advantages account for an improved accuracy and directness in needle placement (5, 6) which results in a more painless procedure for the patient and a reduction in the risk of incidental damage to adjacent structures such as vessels, tendons, nerves and articular cartilage, thus minimising possible adverse events (7). The improved accuracy and safety of US-guided interventions has been eventually linked to better procedural outcomes and to an improvement in joints function in case of intra-articular injections, if compared with palpation-guided or blind procedures (8).

In this review we will discuss the advantages of US-guided interventions, and we will present several practical examples of how US guidance has achieved important results in the rheumatology field in terms of guidance for intra-articular injections, biopsies or in combination with other known techniques such as arthroscopy.

US-guided intra-articular infiltration

Blind or palpation-guided intra-articular injections, even if frequently performed, are associated with a relatively high failure rate due to incorrect needle placement, in particular in case of small joints. Even though synovial fluid aspiration is reported as a valuable predictor of the correct intra-articular placement of drugs in blind procedures, Jones *et al*. observed that only up to half of extra articular injections can be associated with successful aspiration of synovial fluid (9). Moreover, according to three studies that used radiographic contrast to check the accuracy in needle placement of blind injections, the success rate was as low as 42% for glenohumeral joint injections and 32% for tendon sheath injections (9-11).

Conversely, US-guided procedures have reported higher accuracy rate in needle placement compared to clinically-guided injections in several joints such as knee, shoulder, wrist, ankle and elbow, with an accuracy rate of up to 91% (8). A significant improvement in patient's outcome in terms of joints function was also observed in case of accurate corticosteroids (CS) injections compared to inaccurate ones (8). Moreover the higher precision of US-guided injections seem to reduce patients' discomfort and pain, as shown by Sibbit *et al*. who compared US-guided and palpation-guided injections on 148 painful joints, reporting a 43% reduction in procedural pain and a 58% decrease in absolute pain score for sonographic guided interventions (12).

Knee joint

Although injection of knee joint can be readily performed even without image guidance, it is sometimes important to have a confirmation of needle placement, especially in obese individuals, patients with swollen legs or in case of patellar dislocation or arthritis (13, 14). Moreover, while needle placement is easily confirmed when an effusion is present by the return of synovial fluids, without any clinical detectable effusion palpation-guided injections can be inaccurate.

Data report that even for commonly-injected joints such as the knee, the accuracy rate of palpation-guided injections is not so high (nearly 70%) (8, 15) and inaccuracy in needle placement can result in damages to adjacent structures and tissue atrophy within the extra-articular soft tissues, as well as to variable clinical outcomes (15).

Some studies compared US-guided and palpation-guided (or blind) injection in the knee joint, underling the better outcome and higher accuracy rate achieved with the use of US guidance (16, 17).

In a recent study, radiographic imaging was used to compare the accuracy of US-guided *versus* blind intra-articular injections on 126 knees with radiographically-confirmed knee osteoarthritis (OA). Overall, US-guided procedures reported higher accuracy in needle placement and accuracy of the intra-articular injection if compared to blind interventions, with an overall success rate of 96% for the US-guided method *versus* 78% for the blind one. Moreover touching of the patella cartilage or periosteum, which was caused by an incorrect location of the needle tip, was reported only in 3 cases in the US-guided group *versus* 8 cases in the blind group, thus confirming that US-guided injections are safer and more accurate than palpation-guided ones (16).

In another study, the accuracy rate of US-guidance *versus* blind procedure was evaluated in hyaluronic acid knee injections via the suprapatellar bursa, on nearly 100 patients with confirmed knee OA. Also in this case, US-guided interventions resulted in a significant greater accuracy than blind injections (96.0% *vs*. 83.7%), with a good intra-articular delivery and lower incidence of soft tissue infiltration (17).

Hip joints

The accuracy rate of blind or landmarks-guided injection in deep joints such as the hip is considered to be relatively poor (18). This fact, combined with the complexity of the hip anatomy and the proximity of the needle to several neurovascular structures during the injection, makes the employment of image guidance of paramount importance in this type of procedure.

Leopold at al measured the accuracy and safety of blind hip injections on 30 cadavers using methylene blue dye administered anteriorly or laterally. In both cases they reported low accuracy and unreliability of the landmark-based method. Success rate was only 60%–80%, according to the approach used. Moreover the complexity of the hip anatomy resulted in the proximity of the needle tip to the femoral nerve, which was punctured in 27% of lateral injections and in 60% of cases in anterior attempts. In addition, the anterior approach resulted in needle placement really close to other important structures such as femoral artery and femoral cutaneous nerve. The authors concluded that the use of imaging technique can be considered as fundamental to perform hip injections under a proper guidance, in order to avoid injury to the surrounding structures and to achieve higher accuracy in intra-articular needle placement (18).

US-guidance has been increasingly used in hip injections thanks to the possibility to identify, and therefore avoid,

vascular and nervous structures, and increase accuracy and safety of the procedure. The accuracy in needle placement obtained through US-guided procedures has been described in a number of studies in which hip injections were performed using different approaches. In the study by Smith *et al*., 28 patients underwent 30 intra-articular hip US-guided injections through the anterior oblique sagittal approach, reporting a 97% accuracy rate according to fluoroscopy imaging (19). In another study, 10 patients received sodium hyaluronate via US-guided injections, using either a linear array or a curvilinear transducer; the correct placement of the needle into the acetabulum femoral head junction via a parasagittal approach was confirmed by CT and was accurate in 100% of the cases (20). A 100% accuracy rate in needle placement was reported also by Levi, who evaluated the efficacy of a linear array transducer in performing US-guided intra-articular hip injection in 10 patients (21). In Figure 1, we present an example of a US-guided intra-articular injection performed via the antero-superior approach: the needle tip is accurately inserted into the joint capsule on the femoral head.

These results overall suggest that US-guidance can be used to perform complex procedures such as intra-articular hip injections, with good results in terms of accuracy and safety. This kind of approach has already been used to inject different kind of substances like steroids, hyaluronic acid and also platelet-rich plasma (PRP) (22).

Facet joint and atlanto-occipital joint

Intra-articular injections in particular joints, such as facet of atlanto-occipital joints, present some challenges because of the difficulty of the procedure and the high risks resulting from an inaccurate needle tip placement. In this context blind injections are unsafe and unreliable, and the employment of imaging techniques is of paramount importance. US-guidance has proved to be a feasible and reliable method to perform this type of injections, giving good results in terms of accuracy.

Ultrasound devices can be used to guide the injection of anesthetic in facet joints; a procedure used to reveal facet syndrome, a condition that may be accountable for 15–45% of chronic lower back pain (23). Considering that the precision of the injection in the pain-causing joint is fundamental for the success of the procedure, besides the employment of US-guidance adequate training can be provided to ultrasonographers to improve their expertise and skills in this particular intervention. Moult *et al*. reported that students undergoing a specific training for US-guided facet joints injections had improved ability to visualise 3-D needle position and to identify and correct erroneous insertions, reporting an overall success rate of 61.5%, compared to 38.5% achieved by students in the traditional training group (24).

US-guidance can be used also for injections in the atlanto-occipital joint, for which blind procedures are unfeasible due to the anatomic features of this area and the presence of important adjacent structures like vertebral and carotid artery, jugular vein, spinal cord and C1 spinal nerve. In a recent study, the feasibility of US-guided atlanto-occipital joint injection was evaluated in three cadavers, followed by a fluoroscopic assessment of the accuracy of the procedure (25). Despite the difficulties of this type of injection, the authors underline the feasibility of US-guided procedures and especially highlight the fact that Doppler ultrasound is superior to other imaging techniques such as fluoroscopy as it can clearly show vascular structures, thus enabling the operator to advance the needle by avoiding the vessels. In addition, considering that some cases of vertebral artery abnormalities in the atlantoaxial area have been previously reported (26, 27), the real-time visualisation of US devices is fundamental, because even with unexpected anatomic variations needle placement can be adjusted step by step, to achieve the highest level of accuracy (25).

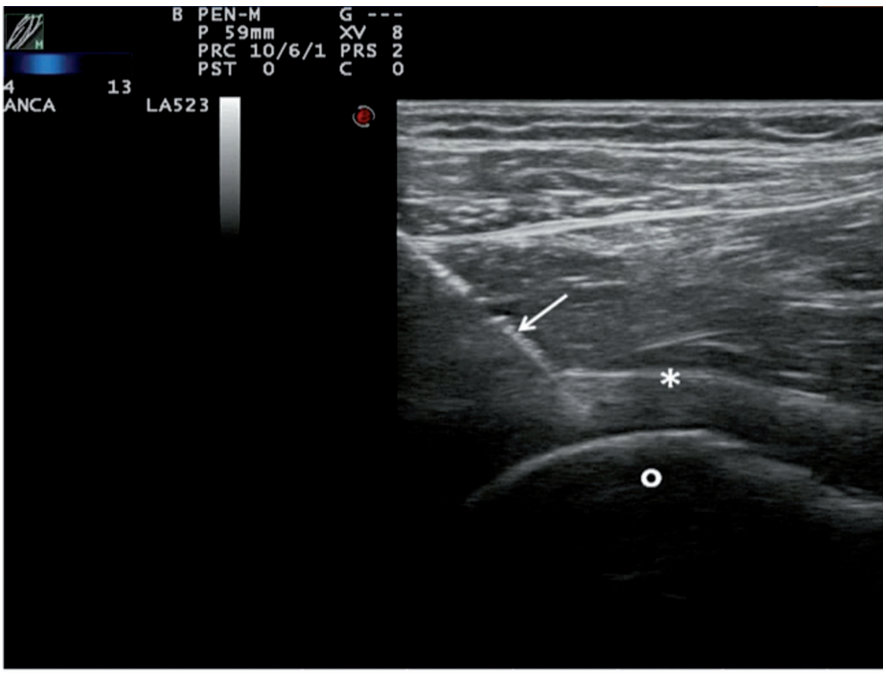

Fig. 1. Ultrasound-guided hip intra-articular injection. The arrow indicates the needle inserted via the antero-superior approach into the joint capsule* on the femoral head°.

US-guided tendon sheaths injections

Different types of tenosynovitis require CS injections to reduce inflammation and to manage pain; in this context the use of US may help guide the injection to the tendon sheath, avoiding errors and needle misplacement which could result in tendon rupture (28).

De Quevain's tenosynovitis affects the first dorsal compartment of the wrist and requires routinely and precise CS injections to achieve symptoms relief. The precision of the injection in patients with this disease is fundamental: two studies showed that in case of

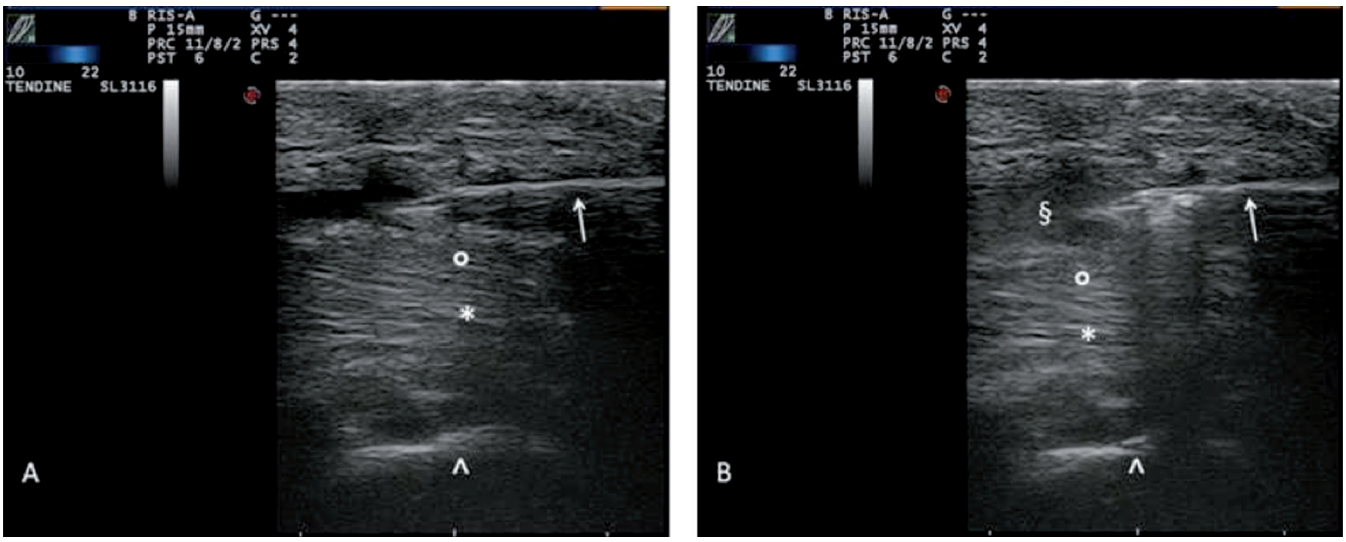

Fig. 2. Ultrasound guided injection into the digital flexor tendon sheath; volar longitudinal scan with 22 MHz probe.
Panel A: the arrow indicates the needle inserted into the superficial° and deep* digital flexor tendon sheaths. The contour of the metacarpal head^ is visible underneath. Panel B: Distention of the tendon sheaths after steroid injection§.

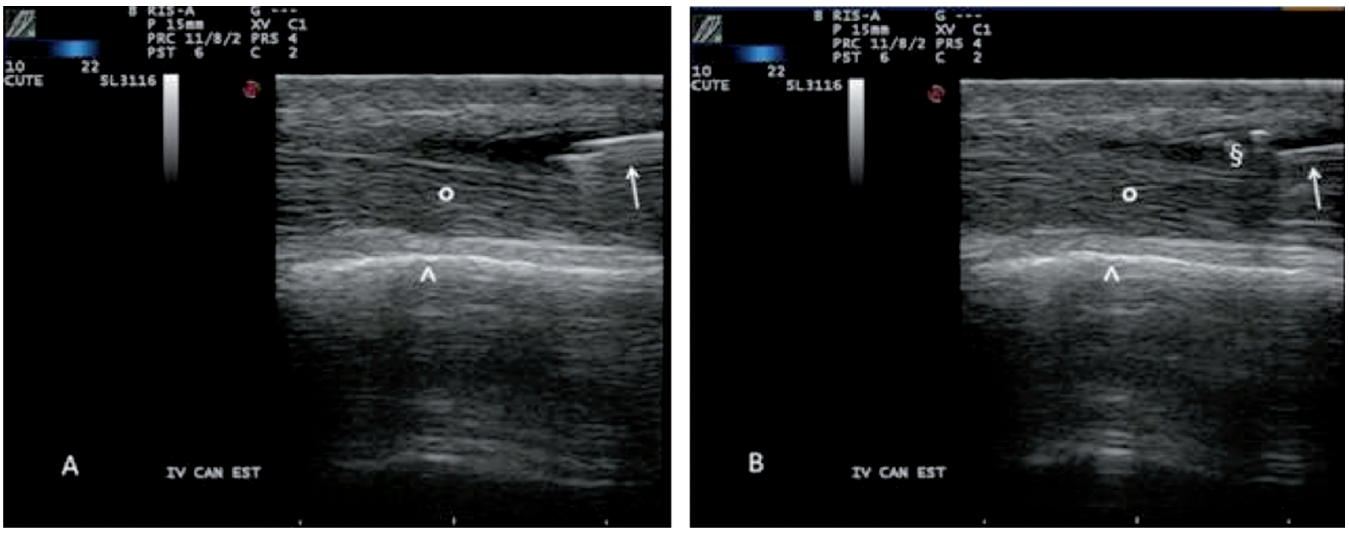

Fig. 3. Ultrasound guided injection into the extensor tendon sheath of the wrist (compartment 4); dorsal longitudinal scan with 22 MHz probe.
Panel A: the arrow indicates the needle inserted into the fourth compartment where the tendons° are visible. The contour of the radial bone^ is visible underneath. Panel B: steroid§ injected into the fourth compartment.

misplaced injections the response was variable and recurrence of symptoms frequent (29, 30). In addition, anatomical variations in the first dorsal compartment are quite common (from 40% to 86%) (31, 32), thus making blind or unguided injections more prone to failure. In a study by McDermott *et al*., 40 patients affected by de Quevain's tenosynovitis were treated with US-guided CS injections (33). The results reported the usefulness of US in documenting septation, observed in 52% of patients. In addition the procedure was successful in 97% of patients, who achieved at least partial resolution of symptoms, while 92% reported near complete resolution (33).

It is worth noting that the correct placement of the needle inside the tendon sheath is practically impossible within blind procedure, while the use of US-guidance enables not only to insert the needle with a higher level of accuracy, but also to reach very small areas such as the superficial and deep digital flexor sheaths (Fig. 2) or specific extensor tendon compartments of the wrist (Fig. 3). Interestingly, US-guidance has been used also to inject enthesis in ankylosing spondylitis patients, demonstrating high effectiveness and safety (34).

US-guided synovial biopsy

The primary site of inflammation in arthritis is the synovial membrane, which can be sampled and analysed in order to obtain useful information on the pathophysiological mechanism, the degree of inflammation and ultimately the prognosis of the disease. There are several possible approaches to synovial tissue sampling, including blind procedure, arthroscopy and US-guided biopsy.

Blind procedure is generally regarded as a simple, inexpensive and well-tolerated method for synovial sampling. However it presents several disadvantages such as the limitation to only larger joints such as the knee joint, the fact that the operator is not able to visually select the tissue under analysis, resulting in potential sampling error, and the fact that it is not always possible to obtain adequate tissue samples, especially in case of investigation of quiescent joints where no inflammation or effusion is present (35).

On the other hand arthroscopic biopsy has been regarded for several years as the gold standard of synovial tissue sampling, in terms of quality and size of specimens (36). Despite the advantages of this technique over the blind procedure, it is still a quite complicated, expensive and invasive method, which is not feasible as a routine procedure due to the need for dedicated personnel and complex instruments.

In the latest decades US has been introduced as a simple and well-tolerated alternative to arthroscopy to guide the sampling of synovial tissue from most patients and most joints (both large and small), thanks to the ability of the ultrasound to detect the needle and all types of instruments, which appear hyperechoic on sonography evaluation. Koski *et al*. reported a method for US-guided synovial biopsy, consisting in the use of set and forcepes, that can be applied to most joints and even bursae and tendon sheaths (37). In addition, another minimally invasive procedure has been described based on the use of a portal and rigid forceps which appear as a reliable method for obtaining synovial samples (38).

Overall US-guided interventions seem to be less invasive and painful than arthroscopy procedures, and according to a recent survey conducted on approximately 100 patients, in 77% of the cases US-guided biopsies are associated to absence of pain during the procedure (39). In addition, the use of US-guidance during biopsy enables the concomitant assessment of synovial thickness through grey-scale score and the evaluation of vascularity, which is associated with active synovial inflammation, through power Doppler. All these elements, combined to the fact that US is inexpensive, easily available in rheumatology units and that it requires less advanced training and facilities if compared to arthroscopy, are leading to the replacement of arthroscopy with US-guided procedures for synovial sampling.

Other possible applications of US-guidance

Combination of US and arthroscopy

The ability of US imaging to give a real-time assessment of joint and tendon movements can be further exploited by combing this method to other techniques already applied in rheumatology. Ultrasound can be for example combined to arthroscopy, as the images produced by each technique are not only comparable, but they provide to the rheumatologist different and complementary information on the anatomy of the joint space (40).

The simultaneous use of US and arthroscopy has been assessed on 11 patients with different rheumatic diseases, who underwent diagnostic or therapeutic synovectomy of the knee (2). Results showed that the combination of the two techniques can be useful both for the arthroscopist to visualise the deeper layers of the synovial membrane, and for the ultrasonographer who can immediately clarify any queries derived from US images, by directly looking at the joint cavity. Thanks to the simultaneous use of the two imaging techniques the performance of arthroscopy can be improved, enabling a better visualisation of the surface and the underlying structure of the synovial membrane and giving a more precise definition of the thickness of the synovial proliferation and its inflammatory status. US-guided arthroscopy seems therefore to result in a more complete, effective and rapid synovectomy, characterised by a more selective and radical resection of the synovial membrane and an improved clinical outcome (2).

Establishment of arthroscopic portals

US-guidance can be also used for the positioning of arthroscopic portals, whose placement is critical for successful and safe arthroscopic surgery. The accuracy in portals establishment is fundamental as it directly impacts on the success and rapidity of the surgical procedure, by assuring a good vision of the surgical zone and optimising access and maneuverability. However, portal placement can be a highly risky procedure because of the proximity of musculotendinous or neurovascular structure and the impossibility for the surgeon to have a direct vision of the structures located between the skin incision and the ending point (41).

The employment of imaging techniques could therefore help surgeons to safely establish arthroscopic portals, especially in case of anatomical complex structures such as the shoulder or the hip. Even though the use of landmark guidance is frequently used for the placement of arthroscopic portals, common directional miscues in the identification of surface landmarks have been reported by a recent study involving 30 independent expert hip arthroscopists (42). Moreover in this study a wide variance was observed between ultrasound guided landmarks and examiner landmarks, therefore suggesting a role for US-guidance in improving accuracy of identification and placement of arthroscopic portals (42).

The employment of US-guidance has been also described by Hua *et al*., who underlined the importance of the real-time ultrasound guidance combined with the use of the arthroscope for the establishment of the anterolateral and anterior hip portals (43).

Safety of US-guided procedures

US-guided interventions are considered as safe and well-tolerated procedures. First of all, they avoid exposure to potentially harmful radiation, used for example in fluoroscopy, or the employment of iodine-based contrast media that may cause allergies (44). Moreover, the higher accuracy in needle placement reduces the risk of damages to structures such as nerves and vessels at the injection site and help avoid local adverse effects that may be caused by the medication or the procedure itself, such as inaccurate CS injections outside the joint cavity.

One possible concern over US-guided procedures is the development of infections; in fact providing an aseptic environment during the intervention is of paramount importance, especially in case of intra-articular injections. A sterile environment can be obtained by cleaning the skin with antiseptic liquids, using sterile gloves, gels and probes covers, and ensuring the passage of the needle only through the cleaned area of skin (45). However according to a study by Cervini *et al*., the incidence of serious infectious complications after different types of US-guided interventions, including fine-needle aspiration, biopsy and injections, is very low, with only 14 procedures-related infections observed over more than 13.000 ultrasound guided interventions performed (46).

The improved accuracy and safety of US-guided procedures *versus* blind ones has also been linked to an increased therapeutic effectiveness of the interventions performed. For example US-guided injections of glucocorticoids has been recommended for patients with painful shoulder with poor response to previous blind injections, given the higher accuracy in medication placement and therefore the better therapeutic outcome that can be achieved through sonographic guidance (47). The same gain in efficacy was reported for patients suffering from wrist pain who underwent US-guided instead of blind injections (48). A greater accuracy in medication delivery linked to a better achievement of US-guidance *versus* blind procedures has been observed especially for small joints, such as foot/ankle and wrist/hand, and for short terms outcomes (<6 weeks), while for larger joints and long-term outcomes results have been controversial and the improvement in function, pain, intensity and range of motion seem to be less dependent of the injection technique (49). Further studies are therefore needed to better evaluate the possible greater effectiveness given by US-guidance also in the long-term and on larger joint spaces.

Conclusions

US-guided interventions are safe and effective procedures, which can improve the precision and therapeutic outcome of several rheumatology interventions.

The employment of US in intra-articular injections leads to higher accuracy in needle placement and medication delivery, which result in better clinical outcome in terms of joint function and decreased risk of damages caused by needle misplacement. The use of US-guidance is not limited to commonly injected joints such as the knee joint; conversely, this technique is fundamental especially in case of complex anatomical areas such as the hip, the facet joint or the atlanto-occipital joint, for which blind procedures are considered inaccurate and unsafe.

US-guidance can also be used in case of synovial biopsies as it improves the visualisation and the evaluation of the inflammatory status of the synovial membrane and it is a rather less invasive, painful and complex procedure if compared to arthroscopy. Moreover, US and arthroscopy can be used simultaneously to increase the efficacy and clinical outcome of procedures such as synovectomy or arthroscopic portals establishment.

Last of all the absence of radiation hazard and the low risk of procedure-related infections, make US-guided procedures rather safe and reliable, provided that some rules are followed on the maintenance of a sterile environment during the intervention.

Overall the main advantages in terms of accuracy, safety and reliability of US-guidance may pave the way for an increased employment of this technique in rheumatology units, and additional studies are expected to further explore the therapeutic advantages of this procedure.

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