

Contrast-Enhanced Ultrasound Determines Supraspinatus Muscle Atrophy After Cuff Repair and Correlates to Functional Shoulder Outcome

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Background: Muscle degeneration as a consequence of rotator cuff tears is mainly assessed by magnetic resonance imaging. Contrast-enhanced ultrasound (CEUS) is a new functional imaging method to assess microvascular perfusion as a fundamental parameter of muscle tissue vitality. In this cross-sectional study, the authors evaluated supraspinatus muscle perfusion after cuff repair and analyzed its association with functional shoulder outcome and the grade of echogenicity in B-mode ultrasound indicating fatty infiltration.

Hypothesis: The authors expected reduced microperfusion of the operated versus the contralateral supraspinatus muscle and a correlation of the muscular microperfusion with functional shoulder outcome.

Study Design: Cross-sectional study; Level of evidence, 3.

Methods: Patients who received unilateral repair of the supraspinatus tendon between 2009 and 2014 were invited for a single followup examination. Functional scores were assessed, including the Constant-Murley score and American Shoulder and Elbow Surgeons score. CEUS examination was performed bilaterally in an oblique sagittal plane of the supraspinatus fossa. Perfusion was quantified by the parameters wash-in perfusion index (WiPI) and peak enhancement via VueBox quantification software. The results of the Constant-Murley score, American Shoulder and Elbow Surgeons score, and perfusion parameters were referenced to the contralateral shoulder. Echogenicity of the supraspinatus muscle was classified with a 3-point scale as compared with the trapezius muscle.

Results: Sixty-seven patients were available, with a mean follow-up of 38.0 ± 18.5 months. Functional assessment showed impaired shoulder function on the operated shoulder as compared with the contralateral side (relative Constant Score [CS], $80\% \pm 19\%$). CEUS revealed diminished perfusion on the operated shoulder (WiPI, $55.1\% \pm 40.2\%$, P < .001). A strong correlation could be demonstrated between the perfusion deficit and functional impairment (relative WiPI and CS: $r_s = .644$, P < .001). Higher grade of echogenicity in B-mode ultrasound was associated with reduced perfusion.

Conclusion: CEUS could visualize impaired supraspinatus muscle perfusion after rotator cuff repair as compared with the contralateral, healthy shoulder. With its ability to quantify microvascular perfusion as a surrogate parameter for muscle vitality and function, CEUS may serve as a quantitative method to evaluate rotator cuff muscles.

Keywords: CEUS; supraspinatus; cuff tear; cuff repair; atrophy; fatty infiltration; Goutallier classification

Rotator cuff tears are among the most common indications in orthopaedic surgery.^{34,36} There has been continuous ambition to determine relevant prognostic factors for a successful postoperative outcome.^{14,27,36,43} The degeneration of rotator cuff muscles after a cuff tear is proposed to play a key role, as it may anticipate the potential of muscles to recover after tendon repair.^{5,7,20,22,23} Goutallier et al²¹ originally described

the fatty infiltration as a radiologic indicator for this muscle degeneration in computed tomography scans, which are nowadays replaced by magnetic resonance imaging (MRI) as the primary imaging choice.^{19,44} Few studies adapted a system for B-mode ultrasound assessment as well.^{24,46,51} So far, those imaging modalities rely on the visible morphologic differences between fat and muscle in intensity and echogenicity, respectively. The translation of MRI-assessed fatty infiltration to clinically useful guidance is still difficult and limited because of insufficient evidence.^{27,40,43} There are controversial opinions about when patients still benefit from an operation or not in case of advanced fatty infiltration.⁴ As a consequence, the perception of orthopaedic surgeons about

The American Journal of Sports Medicine 2018;46(11):2735–2742 DOI: 10.1177/0363546518787266 © 2018 The Author(s)

indications for rotator cuff surgery varies widely and is mainly based on their individual clinical expertise.^{13,34}

The use of contrast-enhanced ultrasound (CEUS) has rapidly spread in clinical routine since the first guidelines in 2004 and their update for nonhepatic applications in 2011.^{1,42} The ultrasound contrast agent SonoVue (Bracco Imaging) consists of sulphur hexafluoride microbubbles about the size of an erythrocyte, which are injected intravenously. Sulphur hexafluoride microbubbles remain intravascular, enhance the blood echogenicity, and depict perfusion on a capillary level. Ultrasound contrast agents are considered very safe with a low incidence of side effects (complication rate <0.001%)⁴¹ and do not demand laboratory testing of renal function before administration. CEUS has already been used for various evaluations of muscle tissue, and its musculoskeletal applications are growing.^{2,10,16,17,55} With its ability to assess microvascular perfusion as a fundamental parameter of muscle tissue vitality and metabolism,^{35,54} CEUS may be a promising new diagnostic tool for the evaluation of rotator cuff muscles and their degenerative process.

In this study, we evaluated the supraspinatus muscle perfusion of patients with unilateral supraspinatus repair. Our primary hypothesis was that the muscle perfusion of the operated shoulder is reduced as compared with the contralateral, healthy side. The association of the supraspinatus muscle perfusion in CEUS was compared with the B-mode echogenicity in ultrasound as a conventional marker of fatty infiltration. Our second hypothesis was that muscular perfusion in CEUS correlates with the functional shoulder outcome. If these hypotheses were to be confirmed, CEUS could be integrated into the diagnostic routine of rotator cuff tears to monitor the degenerative process of muscle tissue and to facilitate the decision process of cuff repair.

METHODS

This study was conducted in accordance with the Declaration of Helsinki in its present form and was approved by the Ethics Committee Heidelberg (S-153/2015). All recruited individuals accorded with the study protocol and gave their written informed consent before any study relevant procedures.

Subjects

A total of 360 patients received repair of the supraspinatus tendon at our institution from July 2009 to July 2014. The operation was performed by 1 of 3 senior orthopaedic surgeons either arthroscopically or via a mini-open technique with a deltoid-splitting approach. If no exclusion criteria applied, patients were invited for a single follow-up examination at least 1 year after the operation.

General exclusion criteria were known intolerance of ultrasound contrast agents (eg sulphur hexafluoride microbubbles), cardiac insufficiency (New York Heart Association III and IV), uncontrollable hypertension, major pulmonary diseases, myocardial infarction, cardiac pacemaker, marcumarization/bleeding disorders, pregnancy, or age <18 years. Patients who had received operations including muscle transfers and proximal humeral plating were also excluded. Patients were included only if the tear was limited to the supraspinatus tendon according to preoperative MRI and documented per intraoperative finding, as additional damage of other rotator cuff muscles may contribute to the impairment of the supraspinatus muscle^{5,22} (Figure 1).

The effects of patient-related data were analyzed by senior trauma surgeon and included age, follow-up, smoking status, and surgical approach on the functional outcome and perfusion.

Clinical Evaluation

Functional assessment consisted of the Constant-Murley score (CS), the American Shoulder and Elbow Surgeons (ASES) score, the DASH questionnaire (Disabilities of the Arm, Shoulder and Hand), and the Simple Shoulder Test.³ Strength measurement for CS was performed with an isometric dynamometer, for which 1 side was attached with a sling to the patient's wrist at 90° abduction of the arm and the other end fixed to the ground. We related the CS of the operated shoulder to the contralateral shoulder to allow interindividual comparisons, previously described as the "individual Constant score" by Fialka et al.¹⁵ This adaptation for age, sex, and constitution was applied for the ASES score as well. Furthermore, an ASES score >80 of the operated shoulder was considered a superior result and $<\!80$ an inferior result.^{8,38,39}

The range of motion was analyzed separately for a correlation of anteversion and abduction with perfusion.

Ultrasound and CEUS Evaluation

All ultrasound examinations were performed bilaterally by the same consultant orthopaedic and trauma surgeon (C.F.) with level III qualification of DEGUM (German society for ultrasound in medicine). The examiner was blinded to any clinical information. An ACUSON S3000 ultrasound device (Siemens Healthineers) was used for all sonographic evaluations, which were standardized for both shoulders.

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One or more of the authors has declared the following potential conflict of interest or source of funding: This study was financially supported by the registered nonprofit association German Society of Ultrasound in Medicine (DEGUM).



Figure 1. Flowchart of study patients. CRPS, complex regional pain syndrome.

The supraspinatus tendon integrity was evaluated with a high-frequency linear transducer (6-18 MHz) in B-mode as previously described.^{18,33,48} The findings were dichotomized such that full-thickness tears were considered retears, while partial-thickness inhomogeneities were clustered with intact tendons.³⁶

The supraspinatus muscle tissue was assessed with a lower-frequency linear transducer (4-9 MHz). Fatty infiltration^{24,46} was classified with the established 3-point scale modified by Wall et al^{51} with regard to echogenicity as compared with the overlying trapezius, visibility of intramuscular tendons, and the muscle pennate pattern. Care was taken to avoid muscle anisotropy by using a highly standardized ultrasound approach (Figure 2).

The CEUS examination was performed in an oblique sagittal plane of the supraspinatus fossa perpendicular to the muscle fibers at the suprascapular notch^{24,46} (Figure 2), since this marks the widest and deepest area of the fossa representing a high muscle:tendon ratio.



Figure 2. Positioning of the linear ultrasound transducer perpendicular to the supraspinatus muscle fibers at the suprascapular notch. Scapular spine and clavicle are marked in blue.

The following standardized settings of the ultrasound device were used in live-dual view (Cadence contrast mode with B-mode): gain, 3 dB; depth, 4.5 cm; dynamic range, 85 dB; mechanical index, 0.09; focus, 4.0 cm. To emphasize and visualize active muscle tissue, patients were instructed to perform a standardized exercise (repeated abduction up to 90° in full pronation with a 1-kg dumbbell for 120 seconds). Immediately after exercise, the arm rested in neutral position with the elbow extended, and a bolus of 4.8 mL of sulphur hexafluoride microbubbles was applied intravenously (cubital vein of the right arm, 20-gauge catheter), directly followed by 10 mL of 0.9% saline solution. At the time of injection, a video clip of 90 seconds with a frame rate of 5 Hz was started and digitally recorded, during which no motion was allowed in order to reduce artifacts.

CEUS Quantification

The CEUS video clip was postprocessed by the ultrasound examiner with the commercially available designated Vue-Box software (v 4.3; Bracco Imaging) to quantify supraspinatus muscle perfusion.

The region of interest was positioned into the supraspinatus fossa, comprising only supraspinatus muscle tissue. To avoid distorting signals, fasciae and larger arteries were excluded. The trapezius muscle was selected by the same criteria as reference tissue following the recommendations of Bracco Imaging and Tang et al.⁴⁷ Time-intensity curves were generated,^{49,50,56} and the following quantified parameters were used for further analysis:

- *Peak enhancement*: the maximum signal intensity of the enhancement curve, reflecting the maximum blood volume in the region of interest (in arbitrary units)
- Wash-in perfusion index (WiPI): area under the curve divided by the wash-in duration of the contrast agent, reflecting the blood inflow per time until peak enhancement (in arbitrary units/second)

Data Analyses

Possible differences of supraspinatus perfusion values between operated and contralateral shoulders were evaluated with the paired t test. Before application of this test, normality of these data was tested according to the Shapiro-Wilk test.

Perfusion values depend on multiple patient-related factors that are not associated with rotator cuff injury and that could disturb objectification in interindividual comparisons.⁴⁷ To minimize these factors, quantified supraspinatus perfusion values were referenced to the trapezius muscle and divided by the perfusion of the contralateral side (WiPI_{supraspinatus}/WiPI_{trapezius})/(WiPI_{contralateral supraspinatus}/WiPI_{contralateral trapezius}). These perfusion ratios were used for the calculation of Spearman correlation coefficients ($r_{\rm s}$) and used as dependent variables in the Wilcoxon U tests for comparisons of independent groups.

The differences in perfusion between groups of echogenicity were evaluated with Kruskal-Wallis analysis. In case of a significant result, a multiple pairwise comparison procedure was performed with the Dwass-Steel-Critchlow-Fligner method. Distributions of retear and grade of fatty infiltration in B-mode ultrasound were calculated by a chi-square test.

The statistical analysis was performed with SAS for Windows (v 9.4; SAS Institute). The empirical distribution of continuous data and scores is reported as mean \pm SD, with absolute and relative frequencies in case of categorical data. A *P* value \leq .05 indicates statistical significance. Whenever it seemed to be essential and possible, data were visualized graphically with Prism software (v 5.0; GraphPad Software).

RESULTS

Patient Characteristics

Of 86 study patients, 15 had to be excluded because of impaired contralateral shoulders. Four patients were excluded because of technical difficulties during the administration of the contrast agent (excessive movement). There were no adverse reactions to sulphur hexafluoride microbubbles.

The mean age of the remaining 67 patients (28 women, 39 men) was 60.3 ± 9.3 years (range, 39-77 years), and the mean follow-up between surgery and examination was 38.0 ± 18.5 months (range, 12-69 years). The mean body mass index (BMI) was 26.7 ± 4.1 , and 29 patients (43.3%) were smokers.

Twenty-six (38.8%) patients received arthroscopic repair of the supraspinatus tendon, with 41 (61.2%) receiving the mini-open technique.

Functional Outcome

On the operated shoulder, the mean CS was 68.0 ± 19.5 , and the mean ASES was 76.1 ± 21.4 ; as compared with the contralateral side, the individual relative scores were $80\% \pm 19\%$ and $80\% \pm 21\%$. The mean DASH and Simple Shoulder Test scores were 15.8 ± 18.7 and 76.8 ± 25.8 . Mean anteversion and abduction were, as compared with the other shoulder, reduced to $158^{\circ} \pm 33^{\circ}$ and $158^{\circ} \pm 38^{\circ}$.

 TABLE 1

 Supraspinatus Muscle Perfusion

 in Contrast-Enhanced Ultrasound, Comparison

 Between Operated and Contralateral Shoulder^a

	Operated	Contralateral	P Value
Total (N = 0	67)		
WiPI	55.1 ± 40.2	98.0 ± 111.0	<.001
\mathbf{PE}	55.3 ± 41.6	98.5 ± 112.3	<.001
Intact $(n =$	46)		
WiPI	63.1 ± 36.3	98.2 ± 90.6	.008
PE	63.2 ± 37.4	98.2 ± 90.0	.008

^{*a*}Intraindividual comparison of the wash-in perfusion index (WiPI) and peak enhancement (PE) between the operated and contralateral shoulders, each related to the ipsilateral trapezius muscle (in mean \pm SD percentages). The patient subgroup with intact supraspinatus tendon repair was compared separately to demonstrate perfusion differences independent of tendon integrity. Supraspinatus muscle perfusion was significantly reduced on the operated shoulders.

Ultrasound

The supraspinatus muscle perfusion of the operated shoulder was significantly lower versus the contralateral side (Table 1, Figure 3). Twenty-one patients (31.3%) suffered from a retear of the supraspinatus tendon and showed significantly lower perfusion when compared with patients with an intact cuff repair (Table 2). To exclude the influence of a retorn tendon on the perfusion analysis, we compared the difference between the operated and contralateral shoulders in the subgroup of patients with an intact reconstruction (n = 46, 68.7\%). The difference in perfusion was lower than that in the analysis including all patients, although still significant (Table 1).

In B-mode, 12 patients did not show increased echogenicity of the supraspinatus muscle, indicating absence of fatty infiltration (grade 0). Thirty-five patients showed grade 1 fatty infiltration, and 20 showed grade 2. The CEUS perfusion differences between these echogenicity groups were significant for grade 0 vs 2 and grade 1 vs 2 but not grade 0 vs 1 (Figure 4). Furthermore, a higher grade of fatty infiltration was associated with a significantly higher retear rate (P = .013) and a significantly lower functional outcome by ASES and CS (data not shown; see the Appendix, available in the online version of this article).

Correlation and Group Comparison of Ultrasound Findings, Functional Outcome, and Patient Characteristics

There was a strong correlation of the supraspinatus muscle perfusion with functional outcome scores and range of motion. Highest correlations could be demonstrated between the relative WiPI and the individual relative CS ($r_{\rm s} = 0.644, P < .001$) as well as the relative ASES ($r_{\rm s} = 0.602, P < .001$) (Table 3). The comparison between



Figure 3. Contrast-enhanced ultrasound images of the trapezius and supraspinatus muscle inside the supraspinatus fossa. Differences between the muscle perfusion on (A) the contralateral, healthy side and (B) the operated shoulder with intact cuff. The regions of interest were placed around the trapezius (purple) and the supraspinatus muscle (green) excluding fasciae and larger arteries. Time-intensity curves were generated by VueBox quantification software. The supraspinatus on the healthy side demonstrated stronger contrast enhancement versus the operated shoulder relative to the perfusion of the trapezius muscle. au, arbitrary unit.

TABLE 2
Supraspinatus Muscle Perfusion
in Contrast-Enhanced Ultrasound,
Comparison Between Intact and Retorn Tendons ^a

	Intact $(n = 46)$	Retear $(n = 21)$	P Value
WiPIrel PErel	$\begin{array}{c} 87.3 \pm 69.1 \\ 87.3 \pm 69.5 \end{array}$	$\begin{array}{c} 43.5 \pm 20.8 \\ 43.2 \pm 21.0 \end{array}$	<.001 <.001

^{*a*}Interindividual comparison of the wash-in perfusion index (WiPIrel) and peak enhancement (PErel) between intact and retorn tendons, each related to the ipsilateral trapezius muscle (in mean \pm SD percentages) and the contralateral shoulder to compensate patient-specific cardiovascular differences. Supraspinatus muscle perfusion was significantly reduced when a retear was present.

patients with superior (n = 34) and inferior (n = 33) outcome demonstrated significant perfusion differences (Table 4, Appendix Videos 1 and 2).

The relative CS and ASES were significantly lower for patients with a retear (CS intact vs retear: $84\% \pm 20\%$ vs $71\% \pm 16\%$, P < .001; ASES intact vs retear: $84\% \pm 20\%$ vs $70\% \pm 19\%$, P = .002).

The functional scores and muscle perfusion neither differed between smokers and nonsmokers nor correlated with age or the follow-up interval. Patients who received arthroscopic supraspinatus repair showed slightly higher CS results, similar ASES values, and slightly lower perfusion when compared with patients operated with the mini-open technique (each P > .05). BMI inversely correlated with



Figure 4. Differences in contrast-enhanced ultrasound supraspinatus muscle perfusion dependent on the grade of echogenicity in B-mode ultrasound as an indicator of fatty infiltration. The perfusion differences between these echogenicity groups were significant for grade 0 vs 2 and grade 1 vs 2. Values are presented as median, interquartile range, minimum, and maximum. WiPIrel, relative wash-in perfusion index.

relative CS ($r_{\rm s} = -0.313$, P = .010), relative ASES ($r_{\rm s} = -0.343$, P = .005), and perfusion, whereas the correlation to the perfusion parameters showed only a tendency to significance (WiPI_{relative}: $r_{\rm s} = -0.237$, P = .054; peak enhancement_{relative}: $r_{\rm s} = -0.229$, P = .063).

TABLE 3
Correlation of the Supraspinatus Muscle Perfusion in Contrast-Enhanced Ultrasound
With the Functional Outcome Scores and Range of Motion $(N = 67)^a$

	CSrel	ASESrel	DASH	SST	Anteversion	Abduction
WiPIrel	.644 (.001)	.602 (.001)	413 (.001)	.454 (.001)	.462 (.001)	.289 (.018)
PErel	.634 (.001)	.597 (.001)	414 (.001)	.454 (.001)	.466 (.001)	.292 (.016)

^aData are provided as correlation (*P* value). Wash-in perfusion index (WiPIrel) and peak enhancement (PErel) were each related to the ipsilateral trapezius muscle and the contralateral shoulder to compensate for patient-specific cardiovascular differences. Constant-Murley score (CSrel) and American Shoulder and Elbow Surgeons score (ASESrel) were each related to the contralateral shoulder. DASH, Disabilities of the Arm, Shoulder and Hand; SST, Simple Shoulder Test. Supraspinatus muscle perfusion correlated strongly with the individual relative CS and ASES.

TABLE 4 Comparison of the Supraspinatus Muscle Perfusion in Contrast-Enhanced Ultrasound Between Patients With

Superior and Inferior Results After Cuff Repair $(N = 67)^a$ Superior (n = 34)Inferior (n = 33)P Value

	I I I I I I I I I I I I I I I I I I I	(/	
WiPIrel PErel	98.2 ± 76.4 98.1 ± 77.0	$\begin{array}{c} 48.2 \pm 22.6 \\ 48.2 \pm 22.9 \end{array}$	<.001 <.001

^aWash-in perfusion index (WiPIrel) and peak enhancement (PErel) were each related to the ipsilateral trapezius muscle and the contralateral shoulder to compensate for patient-specific cardiovascular differences. Patients with superior outcome after cuff repair demonstrated significantly higher supraspinatus muscle perfusion in contrast-enhanced ultrasound. Values are presented as mean \pm SD percentages. ASES, American Shoulder and Elbow Surgeons score. ASES score \geq 80 indicates superior outcome.

DISCUSSION

We investigated the microvascular perfusion of the supraspinatus muscle with CEUS in operated and healthy shoulders and its association to the functional outcome and fatty infiltration. Our results indicate that reduced muscle perfusion may be part of the degenerative process after a cuff tear and reconstruction of the supraspinatus tendon. To our knowledge, this is the first study to demonstrate a correlation of the postoperative supraspinatus muscle fatty infiltration with the functional outcome after cuff repair.

The supraspinatus muscle perfusion was significantly reduced in the operated shoulder versus the contralateral, healthy shoulder, regardless of whether the reconstructed cuff remained intact. Perfusion in CEUS is associated with intramuscular metabolic characteristics and the amount of recruited muscle fibers.^{26,53,54,57} Therefore, the reduced perfusion in the postoperative supraspinatus muscle tissue may directly reflect the altered muscle physiology (deficit in force production of muscle fibers, ultrastructural abnormalities in muscle contractile proteins, accumulation of interstitial and intracellular lipid).^{28,37,45} Furthermore, increased supraspinatus muscle echogenicity as a criterion for fatty infiltration was significantly related to low muscle perfusion in CEUS. This may indicate that the muscular transformation after a rotator cuff tear includes fatty infiltration combined with reduced

microperfusion. Previous investigation of the fatty infiltration of the supraspinatus muscle after cuff repair revealed that further degeneration could be attenuated or stopped as long as the repair remained intact—specifically, that it is not likely to be reversible and proceeds in case of retears.^{5,11,20,32} The fatty infiltration seems to reach a steady state within 1 year postoperatively.²³ Accordingly, we did not find any correlation between perfusion and the time of follow-up in our cohort that was examined at least 1 year after surgery. We confirmed our first hypothesis, that the supraspinatus muscle perfusion was reduced on the operated shoulders as compared with the contralateral sides. Reduced muscle perfusion may be part of the degenerative change of the muscle tissue after supraspinatus tears and reconstruction.

Our second hypothesis-that the shoulder function correlates with the supraspinatus muscle perfusion, as visualized by CEUS-was confirmed as well. Strong perfusion correlated with CS, ASES, DASH, Simple Shoulder Test, and range of motion. The supraspinatus perfusion was twice as high in patients with superior results (ASES >80) as in those with inferior results. We found a negative correlation of BMI with CS and ASES, which corresponds with previous studies.^{25,52} A vascular impairment of the reconstructed tendons in obese patients was discussed by Kluczynski et al.²⁵ This study did not investigate the intratendinous perfusion but did observe lower supraspinatus muscle perfusion in patients with high BMI. Accordingly, previous findings also demonstrated an association between fatty degeneration and BMI.²⁹ Therefore, a possible reason for lower postoperative shoulder function may be reduced muscle tissue quality in obese patients. Further studies are needed to support this hypothesis.

Smoking is known to impair microcirculation,³¹ while the influence of smoking on the functional outcome after rotator cuff surgery is rated inconsistently.⁴³ Interestingly, we found no significant differences between smokers and nonsmokers regarding perfusion or function. Possibly, the effect size of smoking on the microcirculation is not strong and consistent enough to be statistically detected in a relatively small study cohort such as ours. Furthermore, average BMI, being negatively associated with muscle perfusion, was slightly in favor of the smokers (25.9 vs 27.3), therefore potentially counterbalancing a possible reduction of the microcirculation. Age was not associated with function or perfusion. Earlier studies showed that stronger fatty degeneration in the elderly does not necessarily result in worse shoulder function.^{5,27,36,40} The nonconformity of fatty infiltration and perfusion in relation to age needs further verification in prospective trials.

The evaluation of the complex pathophysiologic process of muscle degeneration with MRI and B-mode ultrasound is limited to visible morphologic differences between fat and muscle in intensity and echogenicity, respectively.^{21,51} By using microcirculation as a surrogate parameter for tissue vitality and metabolism. CEUS offers insight into the muscle tissue quality beyond the possibilities of the established imaging modalities. B-mode ultrasound has already proven comparable sensitivity and specificity in the diagnosis of rotator cuff tears.^{12,18,30} whereas in the evaluation of muscle tissue degeneration, MRI is still regarded as the gold standard. CEUS may increase the value of ultrasound-based examinations in this diagnostic field without losing the advantages of time- and cost-effectiveness. The CEUS examination can be rated as semiobjective since its data are quantified with specialized software. In further studies, the progress of muscular degeneration could be monitored on a ratio scale, in contrast to the known ordinal-scaled classifications.^{21,51} As microcirculation in CEUS revealed a strong correlation to the shoulder function, prospective studies should compare preoperative CEUS and MRI examinations as well as the combination of both imaging techniques in their prognostic value to determine the postoperative shoulder function.

This study has several limitations. For reasons of comparability, the presented findings are based on patients with isolated supraspinatus tears, although about 53% of rotator cuff tears include >1 tendon.²² CEUS may be expanded to all rotator cuff muscles, especially the infraspinatus, whose integrity is known to be related to the supraspinatus muscle condition and the clinical outcome 6,20 Furthermore, we included only patients with healthy contralateral shoulders to allow referencing of the quantitative CEUS results.⁴⁷ The observed changes in perfusion cannot be correlated to the preoperative condition or to possible intraoperative muscle trauma,⁹ as no such data were available. Custom-made regions of interest were necessary to exclude fascia and large vessels but may limit the reproducibility of our work. Patients were postoperatively contacted and thus retrospectively recruited for this study, resulting in a low follow-up rate of about 28%, which may include the risk of selection bias.

CONCLUSION

CEUS can visualize impaired supraspinatus muscle perfusion after rotator cuff repair as compared with the contralateral, healthy shoulder. Perfusion correlated strongly with functional postoperative outcome. CEUS is an easily accessible imaging tool that could be integrated into diagnostic routine to monitor the degenerative change of rotator cuff muscles. With its ability to show microvascular perfusion as a surrogate parameter for muscle quality and function, CEUS expands beyond the purely morphologic imaging methods.

ACKNOWLEDGMENT

This study received the Jochen-Löhr-Award of the German Association of Shoulder and Elbow Surgery (DVSE).

A Video Supplement for this article is available online.

REFERENCES

- Albrecht T, Blomley M, Bolondi L, et al. Guidelines for the use of contrast agents in ultrasound: January 2004. Ultraschall Med. 2004; 25(4):249-256.
- Amarteifio E, Wormsbecher S, Krix M, et al. Dynamic contrastenhanced ultrasound and transient arterial occlusion for quantification of arterial perfusion reserve in peripheral arterial disease. *Eur J Radiol.* 2012;81(11):3332-3338.
- 3. Angst F, Schwyzer HK, Aeschlimann A, Simmen BR, Goldhahn J. Measures of adult shoulder function: Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH) and its short version (Quick-DASH), Shoulder Pain and Disability Index (SPADI), American Shoulder and Elbow Surgeons (ASES) Society standardized shoulder assessment form, Constant (Murley) Score (CS), Simple Shoulder Test (SST), Oxford Shoulder Score (OSS), Shoulder Disability Questionnaire (SDQ), and Western Ontario Shoulder Instability Index (WOSI). Arthritis Care Res (Hoboken). 2011;63(suppl 11):S174-S188.
- Burkhart SS, Barth JR, Richards DP, Zlatkin MB, Larsen M. Arthroscopic repair of massive rotator cuff tears with stage 3 and 4 fatty degeneration. *Arthroscopy*. 2007;23(4):347-354.
- Chaudhury S, Dines JS, Delos D, Warren RF, Voigt C, Rodeo SA. Role of fatty infiltration in the pathophysiology and outcomes of rotator cuff tears. *Arthritis Care Res (Hoboken)*. 2012;64(1):76-82.
- Cheung S, Dillon E, Tham SC, et al. The presence of fatty infiltration in the infraspinatus: its relation with the condition of the supraspinatus tendon. *Arthroscopy*. 2011;27(4):463-470.
- Cho NS, Rhee YG. The factors affecting the clinical outcome and integrity of arthroscopically repaired rotator cuff tears of the shoulder. *Clin Orthop Surg.* 2009;1(2):96-104.
- Chung SW, Kim JY, Kim MH, Kim SH, Oh JH. Arthroscopic repair of massive rotator cuff tears: outcome and analysis of factors associated with healing failure or poor postoperative function. *Am J Sports Med.* 2013;41(7):1674-1683.
- Davis ME, Stafford PL, Jergenson MJ, Bedi A, Mendias CL. Muscle fibers are injured at the time of acute and chronic rotator cuff repair. *Clin Orthop Relat Res.* 2015;473(1):226-232.
- De Zordo T, Mlekusch SP, Feuchtner GM, Mur E, Schirmer M, Klauser AS. Value of contrast-enhanced ultrasound in rheumatoid arthritis. *Eur J Radiol*. 2007;64(2):222-230.
- Deniz G, Kose O, Tugay A, Guler F, Turan A. Fatty degeneration and atrophy of the rotator cuff muscles after arthroscopic repair: does it improve, halt or deteriorate? Arch Orthop Trauma Surg. 2014;134(7):985-990.
- Dinnes J, Loveman E, McIntyre L, Waugh N. The effectiveness of diagnostic tests for the assessment of shoulder pain due to soft tissue disorders: a systematic review. *Health Technol Assess.* 2003;7(29):1-166.
- Dunn WR, Schackman BR, Walsh C, et al. Variation in orthopaedic surgeons' perceptions about the indications for rotator cuff surgery. *J Bone Joint Surg Am.* 2005;87(9):1978-1984.
- Fermont AJ, Wolterbeek N, Wessel RN, Baeyens JP, de Bie RA. Prognostic factors for successful recovery after arthroscopic rotator cuff repair: a systematic literature review. J Orthop Sports Phys Ther. 2014;44(3):153-163.
- Fialka C, Oberleitner G, Stampfl P, Brannath W, Hexel M, Vecsei V. Modification of the Constant-Murley shoulder score—introduction of the individual relative Constant score individual shoulder assessment. *Injury*. 2005;36(10):1159-1165.
- Fischer C, Frank M, Kunz P, et al. Dynamic contrast-enhanced ultrasound (CEUS) after open and minimally invasive locked plating of proximal humerus fractures. *Injury*. 2016;47(8):1725-1731.

- Fischer C, Krammer D, Hug A, et al. Dynamic contrast-enhanced ultrasound and elastography assess deltoid muscle integrity after reverse shoulder arthroplasty. J Shoulder Elbow Surg. 2017;26(1):108-117.
- Fischer CA, Weber MA, Neubecker C, Bruckner T, Tanner M, Zeifang F. Ultrasound vs MRI in the assessment of rotator cuff structure prior to shoulder arthroplasty. *J Orthop.* 2015;12(1):23-30.
- Fuchs B, Weishaupt D, Zanetti M, Hodler J, Gerber C. Fatty degeneration of the muscles of the rotator cuff: assessment by computed tomography versus magnetic resonance imaging. *J Shoulder Elbow Surg.* 1999;8(6):599-605.
- Gladstone JN, Bishop JY, Lo IK, Flatow EL. Fatty infiltration and atrophy of the rotator cuff do not improve after rotator cuff repair and correlate with poor functional outcome. *Am J Sports Med.* 2007;35(5):719-728.
- Goutallier D, Postel JM, Bernageau J, Lavau L, Voisin MC. Fatty muscle degeneration in cuff ruptures: pre- and postoperative evaluation by CT scan. *Clin Orthop Relat Res.* 1994;304:78-83.
- Goutallier D, Postel JM, Gleyze P, Leguilloux P, Van Driessche S. Influence of cuff muscle fatty degeneration on anatomic and functional outcomes after simple suture of full-thickness tears. *J Shoulder Elbow Surg.* 2003;12(6):550-554.
- 23. Goutallier D, Postel JM, Radier C, Bernageau J, Zilber S. Long-term functional and structural outcome in patients with intact repairs 1 year after open transosseous rotator cuff repair. *J Shoulder Elbow Surg.* 2009;18(4):521-528.
- Khoury V, Cardinal E, Brassard P. Atrophy and fatty infiltration of the supraspinatus muscle: sonography versus MRI. *AJR Am J Roentgenol.* 2008;190(4):1105-1111.
- Kluczynski MA, Bisson LJ, Marzo JM. Does body mass index affect outcomes of ambulatory knee and shoulder surgery? *Arthroscopy*. 2014;30(7):856-865.
- Krix M, Weber MA, Krakowski-Roosen H, et al. Assessment of skeletal muscle perfusion using contrast-enhanced ultrasonography. J Ultrasound Med. 2005;24(4):431-441.
- Lambers Heerspink FO, Dorrestijn O, van Raay JJ, Diercks RL. Specific patient-related prognostic factors for rotator cuff repair: a systematic review. J Shoulder Elbow Surg. 2014;23(7):1073-1080.
- Laron D, Samagh SP, Liu X, Kim HT, Feeley BT. Muscle degeneration in rotator cuff tears. J Shoulder Elbow Surg. 2012;21(2):164-174.
- Lee S, Lucas RM, Lansdown DA, et al. Magnetic resonance rotator cuff fat fraction and its relationship with tendon tear severity and subject characteristics. *J Shoulder Elbow Surg.* 2015;24(9):1442-1451.
- Lenza M, Buchbinder R, Takwoingi Y, Johnston RV, Hanchard NC, Faloppa F. Magnetic resonance imaging, magnetic resonance arthrography and ultrasonography for assessing rotator cuff tears in people with shoulder pain for whom surgery is being considered. *Cochrane Database Syst Rev.* 2013(9):CD009020.
- Leone A, Landini L. Vascular pathology from smoking: look at the microcirculation! *Curr Vasc Pharmacol*. 2013;11(4):524-530.
- Liem D, Lichtenberg S, Magosch P, Habermeyer P. Magnetic resonance imaging of arthroscopic supraspinatus tendon repair. *J Bone Joint Surg Am*. 2007;89(8):1770-1776.
- Martinoli C. Musculoskeletal ultrasound: technical guidelines. Insights Imaging. 2010;1(3):99-141.
- Matsen FA 3rd. Clinical practice: rotator-cuff failure. N Engl J Med. 2008;358(20):2138-2147.
- Mayevsky A, Manor T, Pevzner E, et al. Tissue spectroscope: a novel in vivo approach to real time monitoring of tissue vitality. *J Biomed Opt.* 2004;9(5):1028-1045.
- McElvany MD, McGoldrick E, Gee AO, Neradilek MB, Matsen FA 3rd. Rotator cuff repair: published evidence on factors associated with repair integrity and clinical outcome. *Am J Sports Med.* 2015;43(2):491-500.
- Mendias CL, Roche SM, Harning JA, et al. Reduced muscle fiber force production and disrupted myofibril architecture in patients with chronic rotator cuff tears. J Shoulder Elbow Surg. 2015;24(1):111-119.
- Namdari S, Donegan RP, Chamberlain AM, Galatz LM, Yamaguchi K, Keener JD. Factors affecting outcome after structural failure of repaired rotator cuff tears. *J Bone Joint Surg Am*. 2014;96(2):99-105.

- Park JY, Chung KT, Yoo MJ. A serial comparison of arthroscopic repairs for partial- and full-thickness rotator cuff tears. *Arthroscopy*. 2004;20(7):705-711.
- Pedowitz RA, Yamaguchi K, Ahmad CS, et al. Optimizing the management of rotator cuff problems. J Am Acad Orthop Surg. 2011;19(6):368-379.
- Piscaglia F, Bolondi L. The safety of Sonovue in abdominal applications: retrospective analysis of 23188 investigations. *Ultrasound Med Biol.* 2006;32(9):1369-1375.
- Piscaglia F, Nolsoe C, Dietrich CF, et al. The EFSUMB guidelines and recommendations on the clinical practice of contrast enhanced ultrasound (CEUS): update 2011 on non-hepatic applications. *Ultraschall Med.* 2012;33(1):33-59.
- Saccomanno MF, Sircana G, Cazzato G, Donati F, Randelli P, Milano G. Prognostic factors influencing the outcome of rotator cuff repair: a systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(12):3809-3819.
- Somerson JS, Hsu JE, Gorbaty JD, Gee AO. Classifications in brief: Goutallier classification of fatty infiltration of the rotator cuff musculature. *Clin Orthop Relat Res.* 2016;474(5):1328-1332.
- 45. Steinbacher P, Tauber M, Kogler S, Stoiber W, Resch H, Sanger AM. Effects of rotator cuff ruptures on the cellular and intracellular composition of the human supraspinatus muscle. *Tissue Cell*. 2010;42(1):37-41.
- Strobel K, Hodler J, Meyer DC, Pfirrmann CW, Pirkl C, Zanetti M. Fatty atrophy of supraspinatus and infraspinatus muscles: accuracy of US. *Radiology*. 2005;237(2):584-589.
- Tang MX, Mulvana H, Gauthier T, et al. Quantitative contrastenhanced ultrasound imaging: a review of sources of variability. *Interface Focus*. 2011;1(4):520-539.
- Teefey SA, Hasan SA, Middleton WD, Patel M, Wright RW, Yamaguchi K. Ultrasonography of the rotator cuff: a comparison of ultrasonographic and arthroscopic findings in one hundred consecutive cases. *J Bone Joint Surg Am.* 2000;82(4):498-504.
- Tranquart F, Mercier L, Frinking P, Gaud E, Arditi M. Perfusion quantification in contrast-enhanced ultrasound (CEUS)—ready for research projects and routine clinical use. *Ultraschall Med.* 2012;33(suppl 1):S31-S38.
- Vitali F, Pfeifer L, Janson C, et al. Quantitative perfusion analysis in pancreatic contrast enhanced ultrasound (DCE-US): a promising tool for the differentiation between autoimmune pancreatitis and pancreatic cancer. *Z Gastroenterol.* 2015;53(10):1175-1181.
- Wall LB, Teefey SA, Middleton WD, et al. Diagnostic performance and reliability of ultrasonography for fatty degeneration of the rotator cuff muscles. J Bone Joint Surg Am. 2012;94(12):e83.
- Warrender WJ, Brown OL, Abboud JA. Outcomes of arthroscopic rotator cuff repairs in obese patients. J Shoulder Elbow Surg. 2011;20(6):961-967.
- Weber MA, Krakowski-Roosen H, Delorme S, et al. Relationship of skeletal muscle perfusion measured by contrast-enhanced ultrasonography to histologic microvascular density. *J Ultrasound Med*. 2006;25(5):583-591.
- Weber MA, Krakowski-Roosen H, Hildebrandt W, et al. Assessment of metabolism and microcirculation of healthy skeletal muscles by magnetic resonance and ultrasound techniques. *J Neuroimaging*. 2007;17(4):323-331.
- Weber MA, Wormsbecher S, Krix M. Contrast-enhanced ultrasound of skeletal muscle [in German]. *Radiologe*. 2011;51(6):497-505.
- Wildner D, Pfeifer L, Goertz RS, et al. Dynamic contrast-enhanced ultrasound (DCE-US) for the characterization of hepatocellular carcinoma and cholangiocellular carcinoma. *Ultraschall Med*. 2014;35(6): 522-527.
- Womack L, Peters D, Barrett EJ, Kaul S, Price W, Lindner JR. Abnormal skeletal muscle capillary recruitment during exercise in patients with type 2 diabetes mellitus and microvascular complications. *J Am Coll Cardiol.* 2009;53(23):2175-2183.

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