FLEX CEUs

Frozen Shoulder

Biological Aspect of Pathophysiology for Frozen Shoulder

It is fairly well understood that frozen shoulder involves several stages, which reflect the series of process from capsular inflammation and fibrosis to spontaneous resolution of this fibrosis. However, the underlying pathophysiologic process remains poorly determined. For this reason, management of frozen shoulder remains controversial. Determining the pathophysiological processes of frozen shoulder is a pivotal milestone in the development of novel treatment for patients with frozen shoulder. This article reviews what is known to date about the biological pathophysiology of frozen shoulder. Although articles for the pathophysiology of frozen shoulder provide inconsistent and inconclusive results, they have suggested both inflammation and fibrosis mediated by cytokines, growth factors, matrix metalloproteinases, and immune cells. Proinflammatory cytokines and growth factors released from immune cells control the action of fibroblast and matrix remodeling is regulated by the matrix metalloproteinases and their inhibitors. To improve our understanding of the disease continuum, better characterizing the biology of these processes at clearly defined stages will be needed. Further basic studies that use standardized protocols are required to more narrowly identify the role of cytokines, growth factors, matrix metalloproteinases, and immune cells. The results of these studies will provide needed clarity into the control mechanism of the pathogenesis of frozen shoulder and help identify new therapeutic targets for its treatment.

1. Introduction

Frozen shoulder (FS) is a common shoulder disease that has progressive loss of shoulder motion and affects 2–5% in the general population [1–4]. FS passes through several stages, which reflect the series of process from capsular inflammation and fibrosis to spontaneous resolution of this fibrosis [5–8]. However, the etiology, pathogenesis, natural course, and most effective treatment of FS still remain controversial.

Arthroscopic and imaging studies have demonstrated that capsular tissue of glenohumeral joint including rotator interval is major pathologic site [8–10]. Rodeo et al. [11] described FS as the process of inflammation and fibrosis. A synovial hyperplasia with increased vascularity presents during an early period, which subsequently leads to fibrosis in the subsynovium and synovium of capsular tissue. This condition initiates as an immune response, which proceeds with inflammatory synovitis and capsular fibrosis [8, 12]. The macroscopic and histological features of the capsular contracture are well defined, but the underlying pathophysiological process remains poorly understood [13].

Recently, many efforts focused on establishing an immune response including inflammatory mediators for FS. The field's understanding of the pathophysiologic mechanisms of FS has been advanced in recent years as a result of basic studies [2, 5, 11, 14–24]. The underlying pathophysiologic processes of FS accompany capsular inflammation with subsequent fibrosis and this is modulated by mediators including inflammatory cytokines, growth factors, enzymes, and matrix metalloproteinases (MMPs) [2, 8, 12]. The

histologic characteristic of FS is a matrix of type I and type III collagen inhabited by fibroblasts and myofibroblasts, which is controlled by an abnormal cytokine production.

Therefore, determining the biological pathophysiology of FS is a pivotal milestone in the development of novel treatment for patients with FS [11]. This article reviews the pathophysiology of FS from a biological perspective.

2. Cytokines and Growth Factors

Inflammatory mediators including interleukin-1α (IL-1α), IL-1β, IL-6, IL-8, tumor necrosis factor-α (TNF-α), cyclooxygenase-1 (COX-1), and COX-2 play a significant role in inflammatory process and collagen catabolism [17]. Several studies have demonstrated that increased expression of inflammatory mediators in the synovial tissue of joint capsule is essential in the pathogenesis of FS (Table 1) [2, 11, 14–17, 25]. An inflammatory cascade induced by abnormal production of inflammatory cytokines is involved in unnatural tissue repair and fibrosis in FS [22]. Cytokines and growth factors control the action of the fibroblast and matrix remodeling is controlled by MMPs and their inhibitors [14]. They play an important part in the transcription of MMPs which control the turnover of connective tissue [14].

Rodeo et al. [11] documented that transforming growth factor-β (TGF-β), platelet-derived growth factor (PDGF), hepatocyte growth factor, IL-1β, and TNF-α have an important role in the synovial hyperplasia and capsular fibrosis in immunohistochemistry (IHC) analyses of capsular tissue of patients with FS. Staining for TGF-β, PDGF, and hepatocyte growth factor was stronger in FS than nonspecific synovitis, which points towards capsular fibrosis in FS. They concluded that TGF-β and PDGF may play a part in the inflammation and fibrosis of the joint capsule in FS and prompt ablation of hypervascular synovitis through corticosteroid injection prevents the progression towards capsular fibrosis.

Lho et al. [2] documented increased expression levels of IL-1α, IL-1β, TNF-α, COX-1, and COX-2 from joint capsule of the FS group compared with the control group. Interestingly, they also observed increased expression levels of IL-1α, TNF-α, and COX-2 in the subacromial bursa of the FS group compared with the control group. When joint fluid was analyzed, increased production of TNF-α and IL-6 was observed. They concluded that increased expressions of inflammatory cytokines in the subacromial bursa as well as joint capsule may be involved in the pain associated with FS and the pathogenesis of inflammation evolving into fibrosis.

Kabbabe et al. [17] documented that mRNA expressions of IL-6 and IL-8 were increased in the joint capsule of FS group. Mullett et al. [22] documented that joint fluid in FS includes inflammatory cytokines and growth factors that stimulate the action of fibroblasts. Ryu et al. [15] reported that the synovium of diabetic FS showed stronger immunostaining to vascular endothelial growth factor (VEGF) and CD34 than synovial tissue from controls. They postulated that VEGF is released in the synovium of diabetic FS and VEGF may play a part in the pathogenesis and neovascularization of diabetic FS.

Bunker et al. [14] reported that mRNA for cytokines and growth factors are present within joint capsule of patients with FS but noted that the frequency was slightly higher compared with the control group. The frequency of positive signals for proinflammatory cytokines such as Il-1β, TNF-α, and TNF-β was not great compared with the tissue of Dupuytren contracture. However, interpretation for these data should be a caution because they did not have statistical analysis between FS and control groups.

3. Matrix Components

Numerous studies have showed that FS is associated with a dense collagen matrix containing fibroblasts and myofibroblasts, suggestive of a fibrotic process [20, 23, 26, 27]. Fibroblastic proliferation of the anterior capsule including rotator interval was identified by immunostaining [23, 27]. Rodeo et al. [11] reported that immunostaining was stronger for type III collagen in anterosuperior capsule from the FS group compared with a control group, reflecting new collagen deposition in joint capsule of FS.

Vimentin is a cytocontractile protein with type III intermediate filaments and a marker of fibroblasts and myofibroblasts [28]. Bunker and Anthony [27] stated that vimentin was highly expressed in capsular tissue and identified that the cells were fibroblasts by immunocytochemistry (ICC). The myofibroblast, or contractile fibroblast, is the pathognomonic cell of contractile scar tissue and can be seen in Dupuytren contracture. Uhthoff and Boileau [23] reported that vimentin was highly expressed in synovial cell and extracellular matrix of the capsule at the rotator interval, coracohumeral ligament, and axillary pouch. However, vimentin was not found in synovial cell or extracellular matrix from posterior capsule. These results suggest that limited shoulder motions in patients with FS are due to capsular contracture of anterior structures as seen by selective expression of vimentin. Uhthoff and Boileau [23] also emphasized the importance of a clear distinguishment between fibroplasia and contracture. Although fibroplasia involved the whole capsular tissue, cytocontractile proteins were only seen in anterior capsule [23]. These data suggest that there is no need to routinely perform a posterior capsular release in patients suffering from primary FS.

Kilian et al. [20] investigated collagen I and III synthesis during the stiffening stage of FS using quantitative reverse transcriptase–polymerase chain reaction (RT-PCR). They found high levels of α1(I) mRNA transcription in samples of FS and Dupuytren contracture. However, the levels of α2(I) and α1(III) chain mRNAs were shown to be similar to normal capsule tissue. Low levels of fibroblast-like cells and α1(III) chains were indicative of a low number of myofibroblasts. These results might be due to myofibroblast apoptosis in the final phase of the fibrosing process.

Kim et al. [21] used oligonucleotide array analysis, real-time RT-PCR, and IHC to show that the levels of intercellular adhesion molecule-1 (ICAM-1, CD54) were significantly greater in capsule from patients with FS compared with controls. ICAM-1 was also significantly increased in the joint fluid and serum of patients with FS compared with normal controls. They concluded that ICAM-1 was increased

Table 1: Results of cytokines and growth factors in reviewed studies.

	Rodeo et al. [11]	Bunker et al. [14]	Ryu et al. [15]	Kanbe et al. [16]	Kabbabe et al. [17]	Lho et al. [2]	A. M. T. Lubis and V. K. Lubis [18]	Cohen et al. [25]
Sample size	19 FS 14 NS, 7 control subjects	14 FS 5 DC, 4 control subjects	11 DFS 5 control subjects	10 FS	13 FS 10 control subjects	14 FS 7 control subjects	50 FS 50 control subjects	9 FS 8 control subjects
Specimen	Capsule	RI	RI	RI	Capsule	Capsule, SAB, joint fluid	Serum	Capsule
Method	IHC	RT-PCR	IHC, Western blot	IHC	RT-PCR	RT-PCR, IHC, ELISA	ELISA	IHC
Cytokine & GF								
IL-1α		(14/14)				↑ (capsule, SAB)		
IL-1β	↑	(6/14)				↑ (capsule)		
IL-6		(14/14)		(++++) (100%)	↑	↑ (joint fluid)		
IL-8					↑			
TNF-α	↑	(1/14)				↑ (capsule, SAB)		
TNF-β		(12/14)						
COX1						↑ (capsule)		
COX2						↑ (capsule, SAB)		
TGF-β	↑	(13/14)					TGF-β1 ↑	Receptor 1 ↑
PDGF	↑	(12/14 for α) (7/14 for β)						
HGF	↑							
FGF		(14/14 for acidic) (12/14 for basic)						
VEGF			↑	(++) (60%)				

in patients with FS, similar to the increase in patients with diabetes mellitus, and may therefore be a therapeutic target for managing FS.

Fibronectin (FN), a glycoprotein encoded by the FN1 gene, is engaged in biological process including cell adhesion, tissue development, and wound healing [29, 30]. FN also has a role in TGF-β regulation [29]. The tenascins (TN), including tenascin R, tenascin C (TNC), and tenascin X, are a highly conserved family of extracellular matrix glycoproteins [25]. TNC has a pivotal role in modulating the actions of TGF-β and is also regulated by TGF-β [31, 32]. TGF-β induces fibroblasts to synthesize, remodel, and contract extracellular matrix, making this cytokine a key mediator of the fibrotic response [33]. Cohen et al. [25] reported that elevated mRNA expression levels of TNC and FN1 are a marker of capsular injury. Upregulation of TGF-β1 receptor I seems to be dependent on symptom duration of FS and TGF-β signaling may be associated with FS. As such, TNC, FN1, and TGF-β1 receptor I may also contribute to inflammation and fibrosis of the capsule.

4. Matrix Metalloproteinases

The MMPs are zinc-dependent proteinases that degrade the matrix as part of natural turnover in normal connective tissue [34]. The synthesis and activity of MMPs are controlled by tissue inhibitor of metalloproteases (TIMPs), cytokines, and growth factors [34]. The MMPs and TIMPs regulate remodeling of extracellular matrix that the fibroblasts produce.

In 1998, Hutchinson et al. [34] documented that MMPs and TIMPs may be associated with the pathogenesis of FS and Dupuytren contracture. A TIMP analogue (Marimastat) was given as an anticancer treatment to patients suffering from gastric cancer. Of the 12 that took the treatment, six had developed bilateral FS within 4 months and three had developed Dupuytren contracture. They postulated the development of FS induced by a lowering of the MMP : TIMP ratio.

Since then, several studies have reported abnormal expression patterns of MMPs and TIMPs that may cause a failure of collagen remodeling in FS (Table 2) [14, 16–19]. Bunker et al. [14] reported that MMP-2 was expressed more frequently than MMP-1 or MMP-3. The membrane-bound MMP-14 is known to have a vital role in MMP-2 activation. The surprising absence of MMP-14 mRNA in all 14 FS specimens suggests a possible mechanism for the slow resolution of fibrosis. In a study by Brown et al. [19], Luminex multiplex analysis was carried out to quantify the levels of MMPs and TIMP-1 in fibroblast cell lines. Production of MMPs 1, 2, 3, and 8 was distinct between groups. MMP-1 production in diabetic FS was significantly reduced compared to FS derived patient cells. Moreover, striking differences were observed when fibroblasts from diabetic FS patients were compared with those from a control group. Calculating MMP-1/TIMP-1 ratios revealed significantly lower ratios in diabetic FS or FS compared with controls. MMPs 7, 9, 12, and 13 were not detected in any of the samples. They concluded that primary FS produces less MMPs and has a smaller MMP/TIMP ratio than controls. These deficiencies in MMP-1 production may reflect an altered capacity for local tissue remodeling.

Kanbe et al. [16] using quantitative IHC documented MMP-3 expression in the vascular and synovial tissues. In a study by Kabbabe et al. [17], quantitative PCR was used to show increased expression levels of (i) MMP-3 and (ii) A disintegrin and metalloproteinase with thrombospondin motifs 4 (ADAMTS 4) as a fibrogenic mediator in a FS group compared with a control group. Xu et al. [35] reported that genetic factors may be involved in FS etiology. They examined single nucleotide polymorphisms in MMP-3 for their association with FS susceptibility and concluded that the MMP-3 rs650108 variant was significantly associated with increased FS susceptibility in a Chinese Han population.

A. M. T. Lubis and V. K. Lubis [18] investigated serum levels of MMPs, TIMPs, and TGF-β1 in FS and normal subjects using ELISA. Baseline MMP-1 and MMP-2 levels were significantly lower, while TIMP-1, TIMP-2, and TGF-β1 levels were significantly higher in FS group than controls. The MMP/TIMP ratio of the FS group was much lower than the control group; this scenario may help contribute to capsular fibrosis in FS.

Considering the results from previous studies, abnormal expression of MMPs and TIMPs may result in a failure of collagen remodeling in FS. However, the results were heterogeneous. Variations in diagnostic criteria, timing of sampling, and technique used for analysis might affect the reported results and conclusions. Further studies using standardized protocols will be needed to better characterize expression of MMPs and TIMPs for determining pathogenesis of excessive fibrosis in patients with FS and to identify new therapeutic targets for its treatment.

5. Immune Factors

An immunological component such as B-lymphocytes, mast cells, and macrophages has also been suggested in FS. Several studies have suggested that FS begins as an immune response which worsens an inflammatory synovitis, subsequently leading to capsular fibrosis [5, 16].

Bunker and Anthony [27] performed IHC for leukocyte common antigen (LCA, CD45) and a macrophages/synovial antigen (PGMI, CD68) to assess their contribution to the inflammatory component. They revealed that leukocytes and macrophages were scarce in capsular tissue and concluded that active fibroblastic proliferation is very akin to those in Dupuytren's contracture, without inflammation and synovial involvement.

Meanwhile, Hand et al. [5] documented the presence of immune cells including B-lymphocytes, T-lymphocytes, and macrophages and mast cells in the synovium and capsule of the rotator interval, suggesting an immune response in FS. Staining with CD3, CD20, CD68, and mast cell tryptase identified these cells. IHC confirmed an inflammatory infiltrate with significant positive staining for CD45 (LCA). Lyve 1 (lymphatics) and S100 (neural marker) antibody staining was frequently positive, demonstrating the presence of lymphatic and nervous tissue, respectively. Mast cells regulate fibroblast proliferation both in vitro and in vivo [5]. The presence of T

Table 2: Results of matrix metalloproteinases in reviewed studies.

	Bunker et al. [14]	Brown et al. [19]	Kanbe et al. [16]	Kabbabe et al. [17]	A. M. T. Lubis and V. K. Lubis [18]
Sample size	14 FS & 5 DD & 4 normal subjects	9 DFS & 9 FS & 9 control subjects	10 FS subjects	13 FS & 10 control subjects	50 FS & 50 control subjects
Specimen	Capsule	RI	RI	Capsule	Serum
Method	RT-PCR	Luminex multiplex analysis	IHC	RT-PCR	ELISA
MMPs					
MMP-1	(9/14)	↓		n.s.	↓
MMP-2	(13/14)	n.s.			↓
MMP-3	(5/14)	n.s.	(+++) (100%)	↑	
MMP-7		(-)			
MMP-8		n.s.			
MMP-9	(8/14)	(-)			
MMP-12		(-)			
MMP-13		(-)		n.s.	
MMP-14	(0/14)				
TIMPs					
TIMP-1	(14/14)	n.s.			↑
TIMP-2					↑
Others					
ADAMTS 4				↑	
ADAMTS 5				n.s.	

and B cells suggests that this mast cell-mediated proliferative fibrosis is an immune-modulated response [5]. More in-depth investigation is required to evaluate these cellular interactions more clearly. Proinflammatory cytokines such as IL-1, IL-6, IL-8, and TNF-α were released from immune cells such as macrophages. This implies a large number of these cells being present in the joint. Kanbe et al. [16] reported that significant positive staining for CD68 was indicative of inflammatory cell.

6. Neuronal and Vascular Factors

Xu et al. [24] documented increased levels of immune-reactive neuronal proteins including growth associated protein 43 (GAP43), protein gene product 9.5 (PGP9.5), and nerve growth factor receptor (P75) in the anterosuperior capsular tissue of glenohumeral joint. These proteins distributed around blood vessels or in fibroblastic tissue. Hand et al. [5] investigated biopsy samples of the rotator interval from 22 patients with FS and found that 17 of 22 samples revealed positive staining for nerve cells (S100). Kanbe et al. [16] reported that peripheral nerve-related proteins, CD56 and S100, were expressed weakly.

Increased vascularity was a common finding demonstrated in histologic and imaging studies of FS. It has been emphasized that neovascularization is pivotal step in its pathogenesis, showing positive immunostaining of VEGF and CD34 [15, 16, 24]. Several studies revealed greater expression of CD34 in joint capsule of an FS group compared to a control group [15, 24].

The results from previous studies imply that neoinnervation and neoangiogenesis in the capsule of glenohumeral joint are crucial events in the pathogenesis of FS and are evidence to explain severe pain experienced by patients with FS.

7. Other Factors

Mechanical stress stimulates mitogen-activated protein (MAP) kinases through cell adhesion molecules such as β1-integrin [36]. MAP kinases can induce cytokine cascade, such as TNF-α or IL-6 expression, which enhances fibroblast proliferation [36]. Kanbe et al. [16] investigated IHC analysis to detect expression of MAP kinases in the synovium of FS. Extracellular signal-regulated kinase (ERK) and Jun N-terminal kinase (JNK) expression levels were increased in the synovial tissue at the rotator interval with positive β1-integrin. Nuclear factor κB (NF-κB), MMP-3, IL-6, and VEGF levels were also higher in the vascular or synovial tissues. They concluded that mechanical stress may transduce cell signaling of MAP kinase by β1-integrin to change cytokines and MMPs in the fibroblasts of FS.

8. Conclusions

Studies characterizing the pathophysiology of FS are inconclusive but suggest both inflammation and fibrosis of the joint capsule mediated by cytokines, growth factors, MMPs, and immune cells. Variations in diagnostic criteria, timing of sampling, and techniques used for these analyses might affect the reported results and conclusions. To enhance our understanding for the disease continuum, better characterizing the biology of these processes at clearly defined stages will be needed. Further basic studies that use standardized protocols are imperative to identify the role of cytokines, growth factors, MMPs, and immune cells. The results of these studies will provide clarity into the control mechanisms of the pathogenesis of FS and help identify new therapeutic targets for its treatment.

Abbreviations

FS:	Frozen shoulder
MMPs:	Matrix metalloproteinases
IL:	Interleukin
TNF:	Tumor necrosis factor
COX:	Cyclooxygenase
TGF:	Transforming growth factor
PDGF:	Platelet-derived growth factor
IHC:	Immunohistochemistry
VEGF:	Vascular endothelial growth factor
ICC:	Immunocytochemistry
RT-PCR:	Reverse transcriptase–polymerase chain reaction
ICAM:	Intercellular adhesion molecule
FN:	Fibronectin
TN:	Tenascin
TNC:	Tenascin C
TIMPs:	Tissue inhibitor of metalloproteases
ADAMTS:	A disintegrin and metalloproteinase with thrombospondin motifs
LCA:	Leukocyte common antigen
GAP:	Growth associated protein
PGP:	Protein gene product
MAP:	Mitogen-activated protein
ERK:	Extracellular signal-regulated kinase
JNK:	Jun N-terminal kinase
NF-κB:	Nuclear factor κB.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] A. I. Binder, D. Y. Bulgen, B. L. Hazleman, and S. Roberts, "Frozen shoulder: A long-term prospective study," *Annals of the Rheumatic Diseases*, vol. 43, no. 3, pp. 361–364, 1984.

[2] Y.-M. Lho, E. Ha, C.-H. Cho et al., "Inflammatory cytokines are overexpressed in the subacromial bursa of frozen shoulder," *Journal of Shoulder and Elbow Surgery*, vol. 22, no. 5, pp. 666–672, 2013.

[3] M. A. Sheridan and J. A. Hannafin, "Upper Extremity: Emphasis on Frozen Shoulder," *Orthopedic Clinics of North America*, vol. 37, no. 4, pp. 531–539, 2006.

[4] J. D. Zuckerman and A. Rokito, "Frozen shoulder: A consensus definition," *Journal of Shoulder and Elbow Surgery*, vol. 20, no. 2, pp. 322–325, 2011.

[5] G. C. R. Hand, N. A. Athanasou, T. Matthews, and A. J. Carr, "The pathology of frozen shoulder," *The Journal of Bone & Joint Surgery (British Volume)*, vol. 89, no. 7, pp. 928–932, 2007.

[6] J. A. Hannafin and T. A. Chiaia, "Adhesive capsulitis: A treatment approach," *Clinical Orthopaedics and Related Research*, no. 372, pp. 95–109, 2000.

[7] B. Saccomanni, "Inflammation and shoulder pain - A perspective on rotator cuff disease, adhesive capsulitis, and osteoarthritis: Conservative treatment," *Clinical Rheumatology*, vol. 28, no. 5, pp. 495–500, 2009.

[8] K. Tamai, M. Akutsu, and Y. Yano, "Primary frozen shoulder: brief review of pathology and imaging abnormalities," *Journal of Orthopaedic Science*, vol. 19, no. 1, pp. 1–5, 2014.

[9] Y. Carrillon, E. Noel, O. Fantino, O. Perrin-Fayolle, and V. A. Tran-Minh, "Magnetic resonance imaging findings in idiopathic adhesive capsulitis of the shoulder," *Revue du Rhumatisme*, vol. 66, no. 4, pp. 201–206, 1999.

[10] W. Zhao, X. Zheng, Y. Liu et al., "An MRI Study of Symptomatic Adhesive Capsulitis," *PLoS ONE*, vol. 7, no. 10, Article ID e47277, 2012.

[11] S. A. Rodeo, J. A. Hannafin, J. Tom, R. F. Warren, and T. L. Wickiewicz, "Immunolocalization of cytokines and their receptors in adhesive capsulitis of the shoulder," *Journal of Orthopaedic Research*, vol. 15, no. 3, pp. 427–436, 1997.

[12] V. Ryan, H. Brown, C. J. Minns Lowe, and J. S. Lewis, "The pathophysiology associated with primary (idiopathic) frozen shoulder: A systematic review," *BMC Musculoskeletal Disorders*, vol. 17, no. 1, article no. 340, 2016.

[13] C. M. Robinson, K. T. M. Seah, Y. H. Chee, P. Hindle, and I. R. Murray, "Frozen shoulder," *The Journal of Bone & Joint Surgery (British Volume)*, vol. 94, no. 1, pp. 1–9, 2012.

[14] T. D. Bunker, J. Reilly, K. S. Baird, and D. L. Hamblen, "Expression of growth factors, cytokines and matrix metalloproteinases in frozen shoulder," *The Journal of Bone & Joint Surgery (British Volume)*, vol. 82, no. 5, pp. 768–773, 2000.

[15] J.-D. Ryu, P. A. Kirpalani, J.-M. Kim, K.-H. Nam, C.-W. Han, and S.-H. Han, "Expression of vascular endothelial growth factor and angiogenesis in the diabetic frozen shoulder," *Journal of Shoulder and Elbow Surgery*, vol. 15, no. 6, pp. 679–685, 2006.

[16] K. Kanbe, K. Inoue, Y. Inoue, and Q. Chen, "Inducement of mitogen-activated protein kinases in frozen shoulders," *Journal of Orthopaedic Science*, vol. 14, no. 1, pp. 56–61, 2009.

[17] B. Kabbabe, S. Ramkumar, and M. Richardson, "Cytogenetic analysis of the pathology of frozen shoulder," *International Journal of Shoulder Surgery*, vol. 4, no. 3, pp. 75–78, 2010.

[18] A. M. T. Lubis and V. K. Lubis, "Matrix metalloproteinase, tissue inhibitor of metalloproteinase and transforming growth factor-beta 1 in frozen shoulder, and their changes as response to intensive stretching and supervised neglect exercise," *Journal of Orthopaedic Science*, vol. 18, no. 4, pp. 519–527, 2013.

[19] I. Brown, I. Kelly, and P. I. McInnes, "Detection of matrix metall oproteinases in primary frozen shoulders," *The Journal of Bone and Joint Surgery. British Volume*, vol. 90-B, supplement II, p. 364, 2008.

[20] O. Kilian, U. Pfeil, S. Wenisch, C. Heiss, R. Kraus, and R. Schnettler, "Enhanced alpha1(I) mRNA expression in frozen shoulder and dupuytren tissue," *European Journal of Medical Research*, vol. 12, no. 12, pp. 585–590, 2007.

[21] Y.-S. Kim, J.-M. Kim, Y.-G. Lee, O.-K. Hong, H.-S. Kwon, and J.-H. Ji, "Intercellular adhesion molecule-1 (ICAM-1, CD54) is increased in adhesive capsulitis," *The Journal of Bone & Joint Surgery*, vol. 95, no. 4, pp. e181–e188, 2013.

[22] H. Mullett, D. Byrne, and J. Colville, "Adhesive capsulitis: Human fibroblast response to shoulder joint aspirate from patients with stage II disease," *Journal of Shoulder and Elbow Surgery*, vol. 16, no. 3, pp. 290–294, 2007.

[23] H. K. Uhthoff and P. Boileau, "Primary frozen shoulder: Global capsular stiffness versus localized contracture," *Clinical Orthopaedics and Related Research*, no. 456, pp. 79–84, 2007.

[24] Y. Xu, F. Bonar, and G. A. C. Murrell, "Enhanced expression of neuronal proteins in idiopathic frozen shoulder," *Journal of Shoulder and Elbow Surgery*, vol. 21, no. 10, pp. 1391–1397, 2012.

[25] C. Cohen, M. F. Leal, P. S. Belangero et al., "The roles of tenascin C and fibronectin 1 in adhesive capsulitis: A pilot gene expression study," *Clinics*, vol. 71, no. 6, pp. 325–331, 2016.

[26] T. D. Bunker, "Frozen shoulder: unravelling the enigma," *Annals of the Royal College of Surgeons of England*, vol. 79, no. 3, pp. 210–213, 1997.

[27] T. D. Bunker and P. P. Anthony, "The pathology of frozen shoulder. A dupuytren-like disease," *The Journal of Bone & Joint Surgery (British Volume)*, vol. 77, no. 5, pp. 677–683, 1995.

[28] A. A. Challa and B. Stefanovic, "A novel role of vimentin filaments: Binding and stabilization of collagen mRNAs," *Molecular and Cellular Biology*, vol. 31, no. 18, pp. 3773–3789, 2011.

[29] S. L. Dallas, P. Sivakumar, C. J. Jones et al., "Fibronectin Regulates Latent Transforming Growth Factor-β (TGFβ) by Controlling Matrix Assembly of Latent TGFβ-binding Protein-1," *The Journal of Biological Chemistry*, vol. 280, no. 19, pp. 18871–18880, 2005.

[30] I. Vakonakis and I. D. Campbell, "Extracellular matrix: from atomic resolution to ultrastructure," *Current Opinion in Cell Biology*, vol. 19, no. 5, pp. 578–583, 2007.

[31] W. A. Carey, G. D. Taylor, W. B. Dean, and J. D. Bristow, "Tenascin-C deficiency attenuates TGF-β-mediated fibrosis following murine lung injury," *American Journal of Physiology-Lung Cellular and Molecular Physiology*, vol. 299, no. 6, pp. L785–L793, 2010.

[32] R. Chiquet-Ehrismann and R. P. Tucker, "Tenascins and the importance of adhesion modulation," *Cold Spring Harbor Perspectives in Biology*, vol. 3, no. 5, 2011.

[33] E. C. LeRoy, M. I. Trojanowska, and E. A. Smith, "Cytokines and human fibrosis.," *European Cytokine Network*, vol. 1, no. 4, pp. 215–219, 1990.

[34] J. W. Hutchinson, G. M. Tierney, S. L. Parsons, and T. R. C. Davis, "Dupuytren's disease and frozen shoulder induced by treatment with a matrix metalloproteinase inhibitor," *The Journal of Bone & Joint Surgery (British Volume)*, vol. 80, no. 5, pp. 907-908, 1998.

[35] Q. Xu, P. Y. Gai, H. L. Lv, G. R. Li, and X. Y. Liu, "Association of MMP3 genotype with susceptibility to frozen shoulder: A case-control study in a Chinese Han population," *Genetics and Molecular Research*, vol. 15, no. 1, 2016.

[36] H. Lal, S. Verma, M. Smith et al., "Stretch-induced MAP kinase activation in cardiac myocytes: Differential regulation through β1-integrin and focal adhesion kinase," *Journal of Molecular and Cellular Cardiology*, vol. 43, no. 2, pp. 137–147, 2007.

The pathophysiology associated with primary (idiopathic) frozen shoulder: A systematic review

Abstract

Background: Frozen shoulder is a common yet poorly understood musculoskeletal condition, which for many, is associated with substantial and protracted morbidity. Understanding the pathology associated with this condition may help to improve management. To date this has not been presented in a systematic fashion. As such, the aim of this review was to summarise the pathological changes associated with this primary frozen shoulder.

Methods: Databases: Medline, Embase, CINAHL, AMED, BNI and the Cochrane Library, were searched from inception to 2nd May, 2014. To be included participants must not have undergone any prior intervention. Two reviewers independently conducted the; searches, screening, data extraction and assessment of Risk of Bias using the Cochrane Risk of Bias Assessment Tool for non-Randomised Studies of Interventions (ACROBAT-NRSI). Only English language publications reporting findings in humans were included. The findings were summarised in narrative format.

Results: Thirteen observational studies (involving 417 shoulders) were included in the review. Eight studies reported magnetic resonance imaging or arthrography findings and 5 recorded histological findings. When reported mean ages of the participants ranged from 40.0 to 59.8 years. Duration of symptoms ranged from 0 to 30 months. The majority of studies ($n = 7$) were assessed to be of moderate risk of bias, two studies at high risk and the remaining four were rated as low risk of bias. Study characteristics were poorly reported and there was widespread variety observed between studies in respect of data collection methods and inclusion criteria employed. Pathological changes in the anterior shoulder joint capsule and related structures were commonly reported. Imaging identified pathological changes occurring in the coracohumeral ligament, axillary fold and rotator interval. Obliteration of the subcoracoid fat triangle also appeared to be pathognomonic. Histological studies were inconclusive but suggested that immune, inflammatory and fibrotic changes where associated with primary frozen shoulder.

Conclusions: This systematic review presents a summary of what is currently known about the tissue pathophysiology of primary frozen shoulder. Further studies that use standardised inclusion and exclusion criteria and investigate changes in naïve tissue at different stages of the condition are required.

Keywords: Frozen Shoulder, Adhesive capsulitis, Systematic review, Imaging, Histology

Background

Although frozen shoulder is considered to be a common musculoskeletal condition, with reviews reporting up to 5.3 % of the population being affected [1], definitive prevalence and incidence rates remain unknown [2]. The condition is associated with; (often severe) pain, sleep deprivation, anxiety, and disability that may be hugely disruptive and impacts on nearly every aspect of daily living [3]. The average duration of the condition is 30.1 months (range 1 to 3.5 years) [4] but it may be substantially longer [5, 6], and the burden placed upon individuals and health care services may therefore be considered substantial [7].

The term "frozen shoulder" was introduced in 1934 by Codman who described the disorder as "difficult to define, difficult to treat and difficult to explain" [8]; and in many respects this remains true today. Frozen Shoulder (FS) has been classified into primary and secondary conditions [9]. Primary FS (PFS) is characterised by an insidious onset of idiopathic origin whereas secondary FS is associated with a defined event, such as a known intrinsic (such as rotator cuff disease) or extrinsic (such as trauma) cause [10]. FS associated with medical conditions such as diabetes and thyroid disorders are subcategorised as secondary systemic frozen shoulder [11].

Symptoms associated with frozen shoulder include: localised pain, pain with movement, night pain (rendering the patient unable to sleep on the affected side), marked limitation of active and passive range of movement (particularly external rotation) and normal shoulder radiograph findings [8]. However, the absence of definitive diagnostic criteria imposes challenges for clinical diagnosis and management and research [12]. This diagnostic challenge is further complicated by the clinical overlap in signs and symptoms between frozen shoulder and other conditions, such as; rotator cuff tendinopathy, calcific tendonitis or early glenohumeral arthrosis [13, 14]. A recent narrative review suggested thickening of the coracohumeral ligament (CHL), joint capsule and synovium to be diagnostic features for frozen shoulder [15]. However no systematic review has yet collated the data from imaging studies to specify the intra and peri-articular changes that are associated with the condition.

Historically, the pathology of FS has been attributed to structures such as the subacromial bursa and joint capsule [16, 17]. As arthroscopic and microbiological techniques have advanced other structures have been associated with the pathogenesis of the condition: namely, the rotator interval (RI), long head of biceps (LHB) and the CHL [18]. Contemporary histological analyses have identified the presence of inflammatory markers within the asscoiated tissue [19]. Cytokines, such as Tumour Necrosis Factor (TNF) α, Interleukin (IL) 1 α and β and IL-6 have also been identified [20]. In addition, studies have reported high numbers of fibroblasts and myofibroblasts, suggestive of a fibrotic process [21, 22]. An immunological component has also been linked with frozen shoulder; such as the presence of B-lymphocytes, mast cells and macrophages [23]. Such studies have led to the suggestion that FS may begin as an immunological response which escalates to an inflammatory synovitis, eventually leading to fibrosis of the capsule and that future research should focus on disease [15].

The purpose of this systematic review was to identify and synthesise the available evidence regarding the intra and peri-articular pathophysiology of primary frozen shoulder. A secondary aim was to identify deficits in our knowledge that may inform future research. The review was designed to include studies that had investigated the pathology, physiology, physiopathology, neurophysiology, histology, histocytochemistry, microbiology, immunochemistry or immunohistochemistry of the glenohumeral joint and its related structures in adults diagnosed with primary frozen shoulder.

Methods

This review is reported in accordance with the PRISMA statement for reporting systematic reviews [24].

Searches

Databases (Medline, Embase, CINAHL, AMED, BNI and the Cochrane Library) were searched from inception until 2nd May, 2014. Searches were performed independently by two researchers (HB and VR). The search strategy was developed using the Population and Intervention component of the PICO formula (Population, Intervention, Comparator and Outcome) [25]. Search terms related to patho-anatomical and pathophysiological changes associated with primary idiopathic frozen shoulder (Table 1). No language restrictions were applied and searches were limited to human studies. In addition to the formal data base searches a reference list search of included publications was also conducted.

Eligibility criteria

Studies were included if the participants were diagnosed as having PFS and had undergone combinations of imaging, histological or biochemical analysis of the glenohumeral joint. Studies were excluded if participants were diagnosed with any form of secondary frozen shoulder, such as diabetes, rotator cuff disease or trauma [12]. To reduce confounding the findings, studies were also excluded if participants had undergone previous interventions directly to the shoulder joint (and were termed non-naïve studies). This was because steroid injections may impact on the structure and biochemistry of the

Table 1 MEDLINE search strategy used in the review

1	SHOULDER JOINT/ (13897)
2	SHOULDER/ (8870)
3	shoulder*.ti,ab. (41413)
4	exp JOINT CAPSULE/ (25623)
5	BURSA, SYNOVIAL/ or CARTILAGE, ARTICULAR/ (23509)
6	LIGAMENTS/ or LIGAMENTS, ARTICULAR/ (17025)
7	subacromial bursa.ti,ab. (207)
8	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (107701)
9	ELBOW/ or KNEE/ or HIP/ or ELBOW JOINT/ or exp KNEE JOINT/ or HIP JOINT/ (89002)
10	8 not 9 (92176)
11	JOINT DISEASES/ or CONTRACTURE/ or exp BURSITIS/ (10137)
12	bursit*.ti,ab. (1880)
13	(adhesive and capsul*).ti,ab. (709)
14	(contracted and shoulder*).ti,ab. (79)
15	(stiff and shoulder*).ti,ab. (220)
16	(restricted and shoulder*).ti,ab. (443)
17	(("50" or fifty) and year and old and shoulder*).ti,ab. (142)
18	contracture*.ti,ab. (15710)
19	(capsular and adhes*).ti,ab. (533)
20	ARTHRALGIA/ (4808)
21	SHOULDER PAIN/ (2817)
22	PERIARTHRITIS/ (1087)
23	(frozen and shoulder*).ti,ab. (862)
24	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (31479)
25	SHOULDER/pa, ph, pp [Pathology, Physiology, Physiopathology] (2414)
26	SHOULDER JOINT/pa, ph, pp [Pathology, Physiology, Physiopathology] (6206)
27	PHYSIOLOGY/ or NEUROPHYSIOLOGY/ (28421)
28	(pathophysiol* or patho-physiol* or physiopathol* or physio-pathol*).ti,ab. (152283)
29	physiology.ti,ab. (78959)
30	HISTOLOGY/ or HISTOCYTOCHEMISTRY/ (74633)
31	(histol* or histop*).ti,ab. (520480)
32	MICROBIOLOGY/ (5837)
33	microbiolog*.ti,ab. (57683)
34	IMMUNOCHEMISTRY/ (9093)
35	IMMUNOHISTOCHEMISTRY/ (246272)
36	immunohistochem*.ti,ab. (236072)
37	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 (1197286)
38	10 and 24 and 37 (1397)
39	limit 38 to humans (1336)

Database: Ovid MEDLINE(R) <1946 to 2nd May 2014>

tissue [15, 26]. Furthermore, arthrographic distension and capsular release are designed to disrupt the capsule [27] and manipulation under anaesthetic (MUA) may cause intra-articular damage to multiple structures [28]. Translation services were not available thus non English language studies, identified through the search, were subsequently excluded.

Selection of studies

Two reviewers (HB and VR) reviewed the articles for eligibility and inclusion with a third reviewer (JL) available in the event of consensus not being achieved. Article titles were used to identify relevant studies. Following this, eligibility was checked and recorded on a checklist designed for the review that incorporated PICO criteria. A data extraction form was developed for the review based upon the University of York, Centre for Reviews and Dissemination (2009) guidance [29].

Data analyses

Following data extraction, the study characteristics were tabulated and the studies synthesized. The variables synthesized in this review were reported findings from imaging studies of the shoulder joint and its related structures, as well as histological, neural and vascular findings. In addition, studies were assessed and their risk of bias appraised. Whether meta-analyses would be possible or appropriate was considered at this point.

Risk of bias

Although not always included in systematic reviews investigating pathophysiological mechanisms it was decided a priori to include an assessment of the risk of bias of the studies included in the current systematic review to enhance the validity of conclusion reached. The choice of a risk of bias tool for the review proved difficult as no one tool was perfectly compatible with this type of review. As the review question did not explore diagnostic accuracy the QUADAS-2 tool to evaluate the risk of bias and applicability of primary diagnostic accuracy studies was not considered appropriate. The ACROBAT-NRSI (A Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions) is used when appraising the risk of bias in non-randomized studies that compares the health effects of at least two interventions. Although the current review explored mechanisms rather than interventions, its domains appeared relevant and appropriate to the review and was chosen for use in the current review [30]. Studies were appraised to be at high, moderate or low risk of bias independently by two reviewers (HB and VR) with a third reviewer available in the event of any non-agreement (JL).

Results

Three thousand five hundred fifty-one potentially relevant studies were identified in searches. Title, abstract and reference list screening identified 58 articles meeting the review criteria. Duplicates (n = 16) were removed and the full text of articles read. Thirteen studies met the inclusion criteria for the review and 29 studies were excluded (Table 2). A summary is provided in the PRISMA flow diagram (Fig. 1). The study characteristics are presented in Table 3.

All 13 included studies were observational in design. Nine studies included a control group [19, 31–38], four did not [14, 39–41]. Of those using a control group, four included patients with rotator cuff pathology [31, 32, 35, 37], three used asymptomatic controls [34, 36, 38] and two studies included patients with shoulder instability [19, 33]. One study included two control groups [31], one with rotator cuff pathology and the other included people without symptoms. Study characteristics were generally poorly reported and there was widespread variation in diagnosis, methods of sample selection, timing of sample selection and presence of confounding variables such as use of oral medications. Eight out of 13 studies (62 %) based their inclusion criteria on the Codman classification [14, 31, 32, 34, 36, 38, 39, 42]. How-ever, it was evident that there were substantial variations in the interpretation of this classification (Table 3).

The risk of bias data is presented in Table 4. The majority of studies (n = 7) were identified as having a moderate risk of bias, with two studies assessed of being at high risk of bias and the remaining four rated as low risk of bias. In general, sample sizes were small, ranging from one to seventy two (average = 28) participants. All studies used convenience sampling. Despite eleven studies identifying potential confounding factors, only six [14, 31, 33–35, 38] reported how they had taken account of them in their study design and/or in their analysis. The risk of bias data and widespread variation between studies did not permit meta-analyses.

Imaging findings

Magnetic resonance imaging (MRI) findings were reported in five studies [14, 31, 32, 34, 38], with one study using Gadolinium enhancement [32] (Table 3). In descending order of frequency, findings included: a substantially thickened CHL [31, 34, 38]; thickening of the joint capsule in the RI [32, 38] and axillary recess [14, 32]; thickening of the synovial membrane in the RI [32] and axillary recess [14, 32]; partial or complete obliteration of the subcoracoid fat triangle [34, 38]; scarring and or thickening of the RI [14, 38]; fluid distension of the bursa within the superior subscapularis recess [31] and synovitis abnormalities around the LHB tendon [38].

Three studies used contrast enhancement arthrography, with two utilising magnetic resonance angiogram (MRA) [35, 36], and the third, radiology [40]. Arthrography findings were contradictory (Table 3). Song et al. [36] reported substantial thickening of the joint capsule in the axillary recess and the RI. Neviaser [40] reported reduced joint capacity secondary to thickening and contracture of the capsule (region unspecified), obliteration of the axillary fold and often complete or near complete abolition of the subscapularis bursa. In contrast, Manton et al. [35] reported a trend for greater capsular thickness in the axillary recess and at the humeral head and increased synovial thickness in the axillary recess in controls, when compared to patients with FS. They also reported that RI abnormalities were more common in control participants, concluding that there are no useful MRA signs of FS.

Histology findings

Extensive histological findings were reported (Table 3). Tissue samples demonstrated the following: a dense collagen matrix and high population of fibroblasts and contractile myofibroblasts [19, 21, 33, 41]; a fibrotic process limited to the anterior part of the capsule [41]; elevated levels of inflammatory cytokines in the SAB and anterior capsule [19] and the presence of mature and regenerating nerve fibres in the anterior capsule [37].

Five studies explored the histological and molecular changes associated with idiopathic FS (Table 5). When the study characteristics were reviewed limitations were evident. As previously identified, symptomology, demographics and the stage of the condition were poorly recorded. Secondly, there was substantial diversity between studies with regards to what was being measured. Furthermore, the techniques used to obtain the data also varied (Table 3).

Neuronal and vascular findings

Xu et al. [37] investigated neuronal changes within the condition. They reported elevated levels of several immunoreactive neuronal proteins (GAP43, PGP9.5 and P75) in the anterosuperior joint capsule. The distribution of these proteins was either close to small blood vessels or within fibroblastic tissue. Increased vascularity was a common feature identified in the histology studies; particularly located in the anterosuperior structures but absent in the inferior structures (with the exception of the AF).

Discussion

Summary of main findings

This review identified that the anterior shoulder structures in primary frozen shoulder were the location of greatest pathological change and in the subsequent

Table 2 List of excluded studies

Reference	Secondary					Injection			Surgery	
	Diabetes mellitus	Trauma	Rotator cuff disease	Biceps tendinopathy	Cause not stated	Distension	Corticosteroid injection	Hyaluronic acid injection	MUA	Arthroscopy
Ahn, K., Kang, C., Oh, Y. & Jeong, W. (2012). Correlation between magnetic resonance imaging and clinical impairment in patients with adhesive capsulitis. *Skeletal Radiology. 41*(10),1301-8.	X									
Bunker T. & Anthony. P. (1995). The pathology of frozen shoulder. A Dupuytren-like disease. *Journal of Bone and Joint Surgery, 77B*(5), 677–683.	X						X			X
Bunker, T., Reilly, J., Baird, K. & Hamblen, D. (2000). Expression of growth factors, cytokines and matrix metalloproteinases in frozen shoulder. *Journal of Bone and Joint Surger,. 82B*(5), 768–773.							X			X
DePalma, A. (1952). Loss of scapulohumeral motion (frozen shoulder). *Annals of Surgery, 135*, 193–204.		X	X	X						
Emig, E., Schweitzer, M., Karasick, D. & Lubowitz, J. (1995). Adhesive capsulitis of the shoulder: MR diagnosis. *American Journal of Roentgenology, 164*(6), 1457–9.										X
Golkalp, G., Algin, O., Yildrim, N. & Yazici, Z. (2011). Adhesive capsulitis: contrast enhanced shoulder MRI findings. *Journal of Medical Imaging and Radiation Oncology, 55*, 119–125.	X									
Gondim Teixeira, P., Balaj, C., Chanson, A., Lecocq, S., Louis, M. & Blum, A. (2012). Adhesive capsulitis of the shoulder: value of inferior glenohumeral ligament signal changes on T2-weighted fat-saturated images. *American Journal of Roentgenology, 198*(6),589-596.					X		X			
Hagiwara, Y., Ando, A., Onoda, Y., Takemura, T., Minowa, T., Hanagata, N. et al. (2012). Coexistence of fibrotic and chondrogenic process in the capsule of idiopathic frozen shoulders. *Osteoarthritis and Cartilage, 20*, 241–249.	X						X			
Hand, G., Athanasou, N., Matthews, T. & Carr, A. (2007). The pathology of frozen shoulder. *The Journal of Bone and Joint Surgery, 89,* 928–932.	X						X			
Jung, J., Jee, W., Chun, H. Kim, Y., Chung, Y. & Kim, J. (2006). Adhesive capsulitis of the shoulder: evaluation with MR arthrography. *European Radiology, 16*(4), 791–796.										X
Kabbabe, B., Ramkumar, S. & Richardson, M. (2010). Cytogenic analysis of the pathology of frozen shoulder. *International Journal of Shoulder Surgery, 4*(3), 75–78.	X									

Table 2 List of excluded studies *(Continued)*

Kanbe, K., Inoue, Y. & Chen, Q. (2009). Inducement of mitogen-activated protein kinases in frozen shoulders. *Journal of Orthopaedic Science, 14*, 56–61.						X		
Kanbe, K., Inoue, K. & Inoue, Y. (2008). Dynamic movement of the long head of the biceps tendon in frozen shoulders. *Journal of orthopaedic surgery, 16*(3), 295–299.	X				X	X		
Kim, Y., Kim, J., Lee, Y., Hong, O., Kwon, H. & Ji, J. (2013). Intercellular adhesion molecule-1 (ICAM-1, CD54) is increased in adhesive capsulitis. *The Journal of Bone and Joint Surgery, 95*(4), e18.	X							
Kim, K., Rhee, K. & Shin, H. (2009). Adhesive capsulitis of the shoulder: dimensions of the rotator interval measured with magnetic resonance arthrography. *Journal of Shoulder & Elbow Surgery, 18*(3), 437–42.								X
Lee, M., Ahn, J., Muhle, C., Kim, S., Park, S., Kim, S. et al. (2003). Adhesive capsulitis of the shoulder diagnosis using magnetic resonance arthrography with arthroscopic findings as the standard. *Journal of computer assisted tomography, 27*, 901–906.							X	X
Lee, S., Park, J. & Song, S. (2012). Correlation of MR Arthrographic findings and range of shoulder motions in patients with frozen shoulder. *Musculoskeletal Imaging, 198*, 173-179								X
Lefevre-Colau, M., Drape, J,. Fayad, F., Rannou, F., Diche, T., Minvielle, F. et al. (2005). Magnetic resonance imaging of shoulders with idiopathic adhesive capsulitis: reliability of measures. *European Radiology, 15*(12), 2415–22.					X			
Loew, M., Heichel, T. & Lehner, B. (2005). Intraarticular lesions in primary frozen shoulder after manipulation under general anaesthetic. *Journal of Shoulder and Elbow Surgery, 14*(1), 16–21.	X				X			
Nago, M., Mitsui, Y., Gotoh, M., Nakama, K., Shirachi, I., Higuchi, F. et al. (2010). Hyaluronan modulates cell proliferation and mRNA expression of adhesion-related procollagens and cytokines in glenohumeral synovial/capsular fibroblasts in adhesive capsulitis. *Journal of Orthopaedic Research*, *28*(6), 726–731.		X			X			
Ogilvie-Harris, D., Biggs, D., Fitsialos, D. & MacKay, M. (1995). The resistant frozen shoulder Manipulation verses arthroscopic release. *Clinical orthopaedics and related research, 319*, 238–248.				X	X			
Omari, A. & Bunker, T. (2001). Open surgical release for frozen shoulder: Surgical findings and results of the release. *Journal of Shoulder and Elbow Surgery, 10*(4), 353–357.	X							

Table 2 List of excluded studies *(Continued)*

Ozaki, J., Nakagawa, Y., Sakurai, G. & Tamai, S. (1989). Recalcitrant chronic adhesive capsulitis of the shoulder. Role of contracture of the coracohumeral ligament and rotator interval in pathogenesis and treatment. *Journal of Bone & Joint Surgery - American Volume, 71*(10), 1511–5.	X			
Reeves, B. (1966). Arthrographic changes in frozen and post-traumatic stiff shoulders. *Proceedings of the Royal Society of Medicine, 59*(9), 827–30.	X			
Rodeo, S., Hannafin, J., Tom, J., Warren, R. & Wickiewicz, T. (1997). Immunolocalization of cytokines and their receptors in adhesive capsulitis of the shoulder. *Journal of Orthopaedic Research, 15*(3), 427–436.			X	
Shaikh, A. & Sundaram, M. (2009). Adhesive capsulitis demonstrated on magnetic resonance imaging. *Orthopedics, 32*(1), 61–62.				X
Tamai, K. & Yamamoto, M. (1997). Abnormal synovium in the frozen shoulder: A preliminary report with dynamic magnetic resonance imaging. *Journal of Shoulder and Elbow Surgery, 6*, 534–543.				X
Uitvlugt, G., Detrisac, D., Johnson, L., Austin, M. & Johnson, C. (1993). Arthroscopic observations before and after manipulation of frozen shoulder. *Arthroscopy, 9*(2),181-5.	X			
Wiley, A. (1991). Arthroscopic appearance of frozen shoulder. *Arthroscopy, 7*(2), 138–143.	X			

Articles that were excluded from the study are listed above. The reasons for exclusion are marked in the relevant column

clinical features of the disease, namely a loss of external rotation of the shoulder. The limited number of studies conducting histological analyses did not permit definitive conclusions pertaining to histological changes associated with PFS, however, and in line with previously published research, immune, inflammatory and fibrosis appear to play a role in the pathological process. The extent to which each component contributes and the variance associated with this cannot as yet be determined.

Clinical inclusion criteria

The review identified substantial variations in interpretation of the Codman classification. Future research must clearly detail defined and standardised diagnostic guidelines, to allow for more accurate and definitive comparisons between findings in studies.

Imaging

Imaging investigations varied substantially across the included trials and are a potential reason for the variations in findings. Three studies used arthrography, with two using direct arthrography, where contrast material was injected directly into the joint [35, 40]. The basis for this is to permit a more precise visualisation of the intra-articular structures [43]. The contrast material was injected until the capsule distended which occurred at approximately 12–14 ml of fluid [44]. Neviaser [17] reported that normal shoulder joint capacity is between 28–35 ml, often reducing to 5–10 ml in cases of FS. Manton et al. [35] reported a tolerance of less than 10 ml in all nine people with FS. Although the significance of reduced joint capacity in the diagnosis of FS remains uncertain [18, 45–47], the effect of capsular distension when introducing the contrast material may have confounded the published findings relating to the capsule and synovium [35, 47]. Song et al. [36] utilised indirect MRA, where contrast was injected intravenously into an antecubital vein. Indirect MRA requires exercising the joint for 10 to 15 min pre-imaging to increase vascular perfusion to improve flow into the joint [48], and again the influence of this activity on the reported findings is unknown.

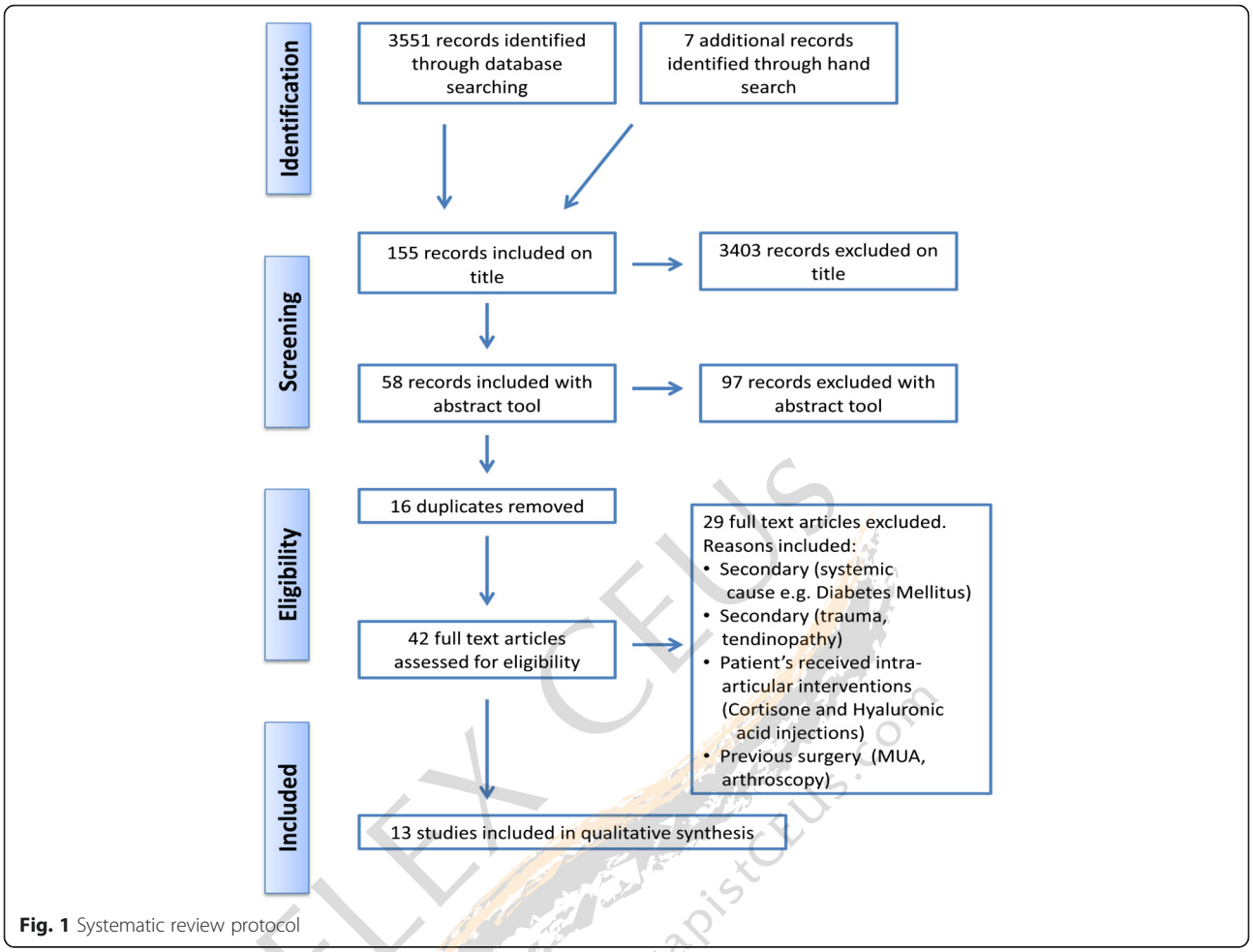

Fig. 1 Systematic review protocol

There is no definitive guidance as to which imaging modality demonstrates greater diagnostic value in FS, and the heterogeneity of techniques used, and their associated potential confounding factors, limits deriving definitive conclusions relating to the articular and peri-articular changes associated with FS.

Histology

Symptomology, demographics and disease stage were poorly reported in the studies included in this review. The widespread diversity between studies with regards to what was being measured and how data was collected made comparison and synthesis of findings difficult. The main findings with respect to pathology identified in this review are presented in Tables 5 and 6 and are summarised below.

Fibrosis and contracture

Bunker [39] and Uhthoff and Boileau [41] used immunocytochemistry (ICC) and immunohistochemistry (IHC) to review matrix components. Both reported fibroblastic proliferation in the superior capsule and the RI. This is consistent with the imaging findings and with previous histological studies [49, 50]. Vimentin is a cytocontractile protein and its presence may be assessed during ICC. Bunker [39] reported that vimentin was strongly expressed and confirmed that the cells were fibroblasts. In addition, when exposed to a smooth-muscle actin, many of the fibroblasts displayed a differentiation into a myofibroblastic phenotype. The myofibroblast, or contractile fibroblast, is the pathognomonic cell of contractile scar tissue and is found in Dupuytren's and the other fibromatoses [51]. Kilian et al. [33] used reverse transcription polymerase chain reaction (RTPCR) to study the mRNA (messenger RNA) transcription rates in the fibrosing stage of FS. They reported decreased levels of fibroblast like cells and α1 (III) chains which was indicative of a low number of myofibroblasts. The differing results may be due to samples being acquired at different stages of disease process; Bunker [39] did not supply information regarding stage of the condition or duration of symptoms since onset so comparison of results is challenging. Discrepancies in data may also relate to the way in which the tissue samples were managed. RTPCR

Table 3 Characteristics of studies included in the review

Authors, date and country of	Sample size and selection	Inclusion and exclusion criteria	Technique used to gain data	Co-morbidities, previous management, naïve tissue	Findings
Bunker, T. [39] United Kingdom	Sample: *N* = 35. Convenience sample. Gender, age, symptom duration and stage of frozen shoulder not reported Control: Nil	Inclusion:"…fitted the criteria for primary frozen shoulder" Exclusion: Not reported	Arthroscopy + Open release	Co-morbidities, previous management and conservative treatment: Not reported. Tissue extracted from patients who failed to manipulate. Naïve tissue: No	Appearance: Consistent abnormality of the subscapularis bursa. Abnormal villous fronding (large, finely divided expansion) of the synovium. Nodular appearance of the synovium. Histology: Tissue consisted of nodules and laminae of dense collagen (mature' type III). Nodules consisted of a collagen matrix containing fibroblasts arranged alongside layers or bundles of dense collagen. The cell population was moderate to high. Increased vascularity (high or moderate) in seven cases. Immunocytochemistry; Vimentin (a cytocontractile protein) was strongly expressed. Myofibroblasts present. Scanty Leukocytes and macrophages (white blood cells). Synovium: (where present) entirely normal or showed minimal papillary infoldings without increased cell production.
Carbone et al. [31] Italy	Sample: *N* = 50. Convenience sample. Gender not reported. Mean age = 57.9 years (SD = 9) Symptom duration: Greater than 6 weeks. Stage: "In the freezing stage" Control: *N* = 65 RC tear *N* = 50	Inclusion: Painful stiff shoulder (6 weeks), severe pain effecting ADL, specific clinical sign of FS, night pain, painful restriction of active & passive elevation to < 100°& ≥ 50 % restriction of external rotation. Exclusion: age < 40 or > 70 year, wider tear than short-wide RC tear and with subscapularis tear, massive fluid distension of S-A space, concomitant RC tear & FS (full passive ROM), previous treatment/ trauma shoulder girdle/ spine.	MRI	Co morbidities: Not reported Previous management: Patients excluded if they had received treatment for shoulder pain—including oral pain relief. Naive tissue: Yes	Appearance: High intensity signal within the superior subscapularis recess, consistent with fluid distension of the bursa, found in 89.95 % of FS patients. The bursa fluid distension was over, in front of and under the coracoid process.
Carrillon et al. [32] France	Sample: *N* = 25. Convenience sample. M:F = 3:22. Mean age = 51 year Symptom duration: 2–10 months (mean = 6 months. Stage: Not reported Control: RC tear *N* = 15	Inclusion: clinical criteria for FS defined by Codman & Lundberg [9]; Gradually increasing shoulder pain, most severe at rest, ≥ 1 month's duration, range of anterior elevation of the shoulder no greater than 135°; range of external rotation no >20° and normal GHJ X-ray (no joint space loss, osteo phytes, or notches). Exclusion: Not reported.	MRI (Gadolinium enhancement)	Co morbidities and previous management: Not reported. Naive tissue: Unknown	Appearance: MRI: Thickening & postgadolinium enhancement (signs of inflammation) of joint capsule and synovial membrane (*n* = 25), RI (*n* = 25) & axillary recess (*n* = 22). No posterior enhancement (signs of inflammation) noted. Postgadolinium enhancement seen in the subacromial bursa (*n* = 18), supraspinatus & infraspinatus tendons (*n* = 9) and ACJ

Table 3 Characteristics of studies included in the review *(Continued)*

					($n = 17$). Normal tendons of subscapularis and LHB in all patients ($n = 25$). Arthroscopy ($n = 2$): Major hemorrhagic thickening of the capsule and synovium at the anterior and inferior part of the joint.
Kilian et al. [33] Germany	Sample: $N = 6$. Convenience sample. Gender, mean age, symptom duration not reported. Stage: "Stage II" (Neviaser classification) Control: Shoulder Instability $N = 6$ Dupytrens $N = 6$	Not reported.	Arthroscopy	Co morbidities: Not reported Previous management: Not reported. Naive tissue: Unknown	Histology: Quantitative Reverse Transcription Polymerase Chain Reaction (Q RT-PCR) Used for quantification of DNA sequences: A significant increase ($P < 0.05$) of α1(I) mRNA chains in FS. The quantity of α2(I) mRNA chains between FS, Dupuytren and normal capsular tissue showed no difference. The α1(III) mRNA transcription rate was similar in FS, Dupuytren and normal capsular tissue capsule. Immunohistochemistry: Decreased numbers of fibroblast-like cells with intracellular procollagen I staining recognisable in FS. Weak staining of collagen I in FS and Dupuytren's tissue when compared to normal capsular tissue. Collagen III staining revealed a corresponding distribution pattern in all 3 groups.
Lho et al. [19] South Korea	Sample: $N = 14$. Convenience sample. Gender, age, symptom duration and stage of frozen shoulder not reported Control: Shoulder Instability $N = 7$	Inclusion: Global restriction shoulder PROM. Arthroscopic confirmation of of hypervascular synovitis& thickened RI &capsule. MRI confirmed no pathology in RI, labrum, LHB or ACJ. Exclusion: Not reported	Arthroscopy	Co morbidities, previous management: Not reported Naive tissue: No	Histology: Elevated IL-1α (Interleukin 1 alpha cytokine) in RI capsule (1.5 +/− 0.15, $P < 0.05$) and SAB (2.3 +/− 0.24, $P < 0.05$), compared to control gp (1.0 +/− 0.01 in joint capsule & 2.0 +/− 0.06 in SAB). Elevated IL-1β (interleukin 1 beta cytokine) in RI capsule only (4.3 +/− 0.3, $P < 0.05$), compared to control gp (3.1 +/− 0.2). Stimulated levels of Tumor necrosis factor alpha cytokine (TNF- α) found in RI capsule (3.1 +/− 0.35, $P < 0.05$) & SAB (3.5 +/− 0.41, $P < 0.01$). Elevated levels of IL-6 (Interleukin 6 cytokine) in SAB only (2.2 +/− 0.3, $P < 0.01$). Cycloogenase COX-1 (enzyme) was increased in the RI capsule only (4.0 +/− 0.14, $P < 0.05$). Cycloogenase COX-2 (enzyme) was increased in the RI capsule (5.0 +/− 0.15, $P < 0.05$) and SAB (6.9 +/− 0 .94,

Table 3 Characteristics of studies included in the review *(Continued)*

					$P < 0.05$) (but not in controls). TNF-α and IL-6 were increased in joint fluid: TNF-α level higher in FS (16.0 +/− 4.04 pg/mL (picograms per millilitre) than controls (10.0 +/− 1.76 pg/mL) ($P < 0.05$). Increased production of IL-6 in FS (21.8 +/− 4.63 pg/mL) compared to controls (3.7 +/− 0.42 pg/mL) ($P < 0.05$).
Li et al. [34] China	Sample: $N = 72$. M:F = 22:50. Convenience sample. Mean age = 53.5 years Symptom duration: 15 weeks—18 months (mean = 9.1 months). Stage: Not reported. Control: $N = 120$	Inclusion: "Clinical evidence of FS". Insidious onset pain & dysfunction. Clinical criteria; increasing pain &stiffness >15 weeks, most severe at rest with restriction of PROM > 30° for 2 or more planes of movement. Exclusion: Previous trauma or shoulder surgery, tumours, RC tear, Calcium deposit on radiography, rheumatoid Arthritis, osteoarthritis, diabetes mellitus, thyroid/heart/ pulmonary/cervical disease, stroke.	MRI	Co morbidities: Excluded. Previous management: All had undergone medical treatment including anti-inflammatory medication, +/− physiotherapy followed up for 24 months. Naive tissue: No	Appearance: Findings in the FS group, but not in control group:1. High-signal intensity soft tissue in the rotator cuff interval. 2. A thickened inferior glenohumeral ligament (axillary recess).3. A low-signal intensity thickened CHL. The CHL was not visualised in 10 out of 120 shoulders in the control group (8.3 %), and 15 out of 72 shoulders in the frozen shoulder group (20.8 %) ($P < 0.05$). The CHL thickness in FS (3.99+/− 1.68 mm) was significantly > control group (3.08+/−1.32 mm), ($P < 0.001$).
Manton et al. [35] United States of America	Sample: $N = 9$. M:F = 7:2. Convenience (retrospective) sampling Mean age = 40 year Symptom duration and stage: Not reported Control: Suspected RC or labral pathology $N = 19$	Inclusion: Arthrographic diagnosis of ≥2 of: Joint volume < 10 ml, poor /absent filling of axillary recess of the joint or biceps tendon sheath, irregularity of capsule insertion, pain after injection of <10 ml of contrast material, or extravasation of contrast material prior to injection of 10 ml or more. Exclusion: Not reported	Direct MRA (Intra-articular Gadopentetate Dimeglumine)	Co morbidities: Not reported. Previous management: No distention or anti-inflammatory injection performed before MRI. Naive tissue: No	Appearance: No SD in amount of fluid in the biceps tendon sheath ($P = 0.45$) or the axillary recess ($P = 0.37$) between FS and controls. No corrugation of the synovium in FS, (In controls n = 7). No abnormalities of the rotator interval capsule in FS (In controls $n = 7$). The average thickness of the synovium and capsule at the axillary recess was 4.1 mm (FS) and 5.1 mm (controls) ($P = 0.11$). The mean thickness of the capsule at the humeral head was 3.0 mm (FS) and 4.0 mm (controls) ($P = 0.07$).
Neviaser, J. [40] United States of America	Sample: $N = 53$ Case series (1 case study). Gender, age, symptom duration and stage of frozen shoulder not reported Control: Nil	Not reported.	Arthrography (Radiographic examination) (Intra-articular Diodrast)	Co morbidities and previous management: Not reported Naive tissue: Unknown	Appearance: Thickening and contracture of capsule with resultant decrease injoint capacity and adherence of the reflected fold causing obliteration of the dependent axillary fold. 42/53 patients had decreased joint capacity, obliteration of the axillary fold and frequently a complete/ almost complete

Table 3 Characteristics of studies included in the review *(Continued)*

					absence of the subscapularis bursa. In every case there was In some instances the subscapularis bursa was obliterated and could not be visualised. The biceps sheath was outlined in the majority of pts. Only 18 % of the shoulders with proved FS showed failure of visualisation of the biceps sheath by arthrogram.
Sofka et al. [14] United States of America	Sample: $N = 47$ M:F = 13:33. Convenience sample Mean age = 53 years Symptom duration and clinical staging: Stage 1:(0–3 months) $n = 8$ Stage 2:(3–9 months) $n = 23$ Stage 3:(9–15 months) $n = 8$ Stage 4:(15–24 months) $n = 8$ Control: Nil	Inclusion:".....either the presumptive clinical diagnosis of FS or MRI findings suggestive of FS". Exclusion: Not reported	MRI	Co-morbidities and previous management: Not reported Naive tissue: Unknown	Appearance: Thickening of the axillary pouch ranged from 2–13 mm (average = 7 mm). All subjects demonstrated RI scarring, (mild $n = 16$,moderate $n = 26$, severe = $n = 5$). No SD between the degree of scarring between gps. Analysis of signal intensity of the capsule included $n = 5$ with isointensity (the same intensity), 13 with hypointensity, and 29 with hyperintensity relative to the normal signal of shoulder capsule. Capsular and synovial thickening (in the axillary pouch) demonstrated the most correlation with clinical stage of FS with a mean axillary pouch thickness for; stage 2 (7.5 mm), stage 1 (4.1 mm), stage 3 (5.5 mm), and stage 4 (4.1 mm) ($P < 0.05$). No SD for values for stages 1, 3, and 4 when compared to each other. Evaluation of capsular signal was significant ($P = 0.02$), with hyperintense signal correlating with stage 2.
Song et al. [36] Korea	Sample: N =35. M:F = 14:21. Convenience sample. Mean age = 50.1 year Symptom duration: At least 4 weeks. Stage: Not reported Control: $N = 45$	Inclusion: Clinical Diagnosis: painful stiff shoulder for ≥ 4 weeks, severe shoulder pain affecting ADL/work, night pain, painful restriction of active and passive elevation to < 100°, 50 % restriction of external rotation, normal radiologic appearance, no secondary causes. Exclusion: RC tear, calcium deposition on radiograph. Bony abnormalities, such as # of clavicle/ greater tuberosity of the humerus and bony Bankart lesion, shoulder surgery, or > than specified ROM.	Indirect MRA (Intra-venous Gadobutrol)	Co-morbidities and previous management: Not reported. Naive tissue: Unknown	Appearance: FS patients had a significantly thicker joint capsule (5.9 +/− 1.7) in the axillary recess and a significantly thicker enhancing portion (6.5 +/− 2.5) of the axillary recess and of the RI (8.3 +/− 3.4) than control gp (4.2 +/− 1.7; 2.1 +/− 3.0; 3.0 +/− 3.6) ($P < 0.001$). 5 pts with FS (14 %) and 7 controls (16 %) had subacromial bursitis ($P = 1.0$). 3 pts with FS (9 %) and 7 controls (16 %) had OA of the ACJ ($P = 0.5$). No glenohumeral

Table 3 Characteristics of studies included in the review *(Continued)*

					joint effusion was observed in 29 of 35 patients with FS (83 %).
Uhthoff & Boileau [41] France	Sample: $N = 4$. M;F = 0:4. Convenience sample. Mean age = 60 year Symptom duration: 12 months. Stage: Not reported Control: Nil	Not reported	Arthroscopy	Dupuytren's ($n = 1$) Previous management: Not reported Naive tissue: Unknown	Appearance: Marked synovial reaction of the GHJ. Histology: Little difference in histological findings in synovial tissue & the extracellular matrix of the posterior & anterior structures. Site of biopsy;(1) synovial tissue & capsule from the posterosuperior part of the joint ($n = 4$); (2) synovial tissue and capsule at the RI ($n = 4$); (3) tissue from the CHL ($n = 4$); (4) synovial tissue and capsule from the axillary fold ($n = 2$); and (5) synovial tissue and inferior capsule in contact with the axillary nerve ($n = 1$). Vimentin (a cytocontractile protein) expression in synovial and endothelial cells was similar at the level of the posterosuperior site and the RI. Vimentin was strongly expressed in cells and extracellular matrix of the capsule at the RI, the CHL, and the axillary fold. No expression for vimentin was detected in cells or in the extracellular matrix from posterosuperior capsule specimens. Desmin not expressed in any section. A marked synovial vascular reaction accompanied by formation of villi was found at all sites (intensity varied among different locations). Presence of fibroplasia was evident at all surgically released sites, and areas of spatially nonaligned type III collagen, containing an increased number of fibroblasts, were separated by strands of spatially aligned type I collagen containing the typical fibrocytes in nearly normal numbers. The simultaneous presence of types I and III collagen was similar at all released sites with the exception of the inferior capsule in which little type III collagen was found. Signs of

Table 3 Characteristics of studies included in the review *(Continued)*

					inflammation or perivascular infiltration were not detected in any section.
Xu et al. [37] Australia	Sample: $N = 8$. M:F = 5:3. Sample: Unclear. Mean age = 58 years Symptom duration: 4–9 months (mean = 6.3 months). Stage: Not reported Control: RC pathology $N = 10$	Inclusion: Pain at night and rest. Radiograph = normal. Decreased ROM under anaesthetic. Evidence of synovial fibroblastic proliferation & associated fibrosis on histological examination of biopsy samples. Exclusion: Previous surgery, radiographic signs of shoulder girdle #, Rheumatoid Arthritis, pts with FS & RC tear at same time.	Arthroscopy	Co morbidities and previous management: Not reported. Naive tissue: Unknown	Appearance: Capsular tissue from FS patients was thickened and hyperaemic. Subsynovial hypercellularity was noted, with fibroblastic proliferation and associated variable, focally prominent collagen production and fibrosis. Associated prominent small vascular channels and vascular congestion was seen. [In RC tissue, plump connective tissue cells in a loose fibrous stroma were noted, vascular proliferation was not present, and fibroblastic proliferation with fibrosis was not evident.]. PGP9.5 (a pan-neuronal marker) and GAP43 (a neuronal membrane protein, nerve marker) immunoreactions: The immunoreactivity pattern of distribution of the nerve markers PGP9.5 and GAP43 was similar in capsular tissue from FS and from controls– Both were mainly seen in the subsynovial tissue adjacent to blood vessels. In the FS tissue, PGP9.5 nerve fibres were often observed close to small blood vessels and within the fibroblastic tissue. The expression of PGP9.5 and GAP43 was significantly higher in FS samples (2.8 +/− 0.2 and 2.4 +/− 0.4 per field) than in rotator cuff tear samples (1.6 +/− 0.6 and 1.3 +/− 0.4 per field, $P < 0.05$). CD34 (a blood vessel marker) immunoreactions: CD34 was strongly expressed in the capsular tissue in 6 FS patients (75 %) but in only 1 rotator cuff tear patient (10 %), supporting increased vascularity in the FS samples. Increased subsynovial vascularity and increased numbers of plump fibroblasts were observed in FS compared with RC patients. Vascular proliferation and congestion in the subsynovial fibrous tissue was seen only in FS.P75 (a nerve growth factor (NGF) receptor - neurotrophin

Table 3 Characteristics of studies included in the review *(Continued)*

					receptor) immunoreactions:P75 was expressed in vascular adventitia (the outer most connective tissue) and nerve fibres around blood vessels and was frequently seen in the subsynovial tissue. Although not everywhere, increased expression of P75 was observed in the FS samples compared with RC patients. Moderate to strong staining for P75 antibody was noted in the capsular tissue in 100 % of FS but only in 30 % of RC samples.
Zhao et al. [38] China	Sample: *N* = 60 M:F = 24:36. Sample: Unclear. Mean age = 50.2 years Symptom duration: 15 weeks - 30 months (mean = 12 months) Stage: "Patients were classified into early or late stage" Further details unclear. Control: *N* = 60	Inclusion: Clinically diagnosed with FS, insidious onset of pain and dysfunction. Clinical criteria: increasing pain and stiffness for > 15 weeks, most severe at rest, with restriction of PROM greater than 30° in two or more planes of movement. Exclusion: Previous surgery or trauma. Neurological disorder involving the upper limbs. Clinical history and clinical examination compatible with RC tear. Presence of calcium deposition on radiographic evaluation, Rheumatoid arthritis, Osteoarthritis.	MRI	Co morbidities: Not reported Previous management: Not reported Naive tissue: Unknown	Appearance: FS pts had a significantly thicker CHL (4.21 mm +/− 0.97) than control subjects (2.12 mm +/− 0.84, $P < 0.001$). Mean thickness of the articular capsule at the RC interval > in FS pts (7.20 mm +/− 2.13) than in controls (4.43 mm +/− 1.16, $P < 0.05$). Partial or complete obliteration of the subcoracoid fat triangle ("subcoracoid triangle sign") was significantly more frequent in FS pts compared with control subjects (partial obliteration, 22 vs. 2 cases (73 % vs. 13 %); complete obliteration, 8 vs. 1 cases (26 % vs. 1.6 %), $P < 0.001$. Synovitis-like abnormalities around the long biceps tendon were also markedly more frequent in patients than in control subjects (18 vs. 2 cases (60 % vs. 6 %), $P < 0.05$. Patients were not significantly different from control subjects with regard to synovitis-like abnormalities at the articular surface of the subscapularis tendon or in the supraspinatus muscle tendon.

RC Rotator Cuff, *ADL* Activities of daily living, *yrs* Years, *FS* Frozen shoulder, *pts* Patients, *CHL* Coracohumeral ligament, # Fracture, *ROM* range of movement, *GHJ* Glenohumeral joint, *RI* Rotator interval, *OA* Osteoarthritis, *ACJ* Acromioclavicular joint, *MRI* Magnetic resonance imaging, *MRA* Magnetic resonance arthrogram

Table 4 Risk of bias results for the studies included in the review

	Bunker [39]	Carbone et al. [31]	Carrillon et al. [32]	Kilian et al. [33]	Lho et al. [19]	Li et al. [34]	Manton et al. [35]	Neviaser [40]	Sofka et al. [14]	Song et al. [36]	Uhthoff & Boileau [41]	Xu et al. [37]	Zhao et al. [38]
1. Did the study address a clearly focused issue?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Did the authors use an appropriate method to answer their question?	Yes Arthroscopy and Open Release	Yes MRI – No comment on contrast	Yes MRI - Contrast	Yes Arthroscopy	Yes Arthroscopy	Yes MRI – No comment on contrast	Yes Direct MRA	Yes Arthrography	Yes MRI – No Comment On Contrast	Yes Indirect MRI	Yes Arthroscopy	Yes Arthroscopy	Yes MRI– No Comment On Contrast
3. Were the cases recruited in an acceptable way?	No SoC *N* = 35	Yes SoC *N* = 50	Yes SoC *N* = 25	No SoC *N* = 6	No SoC *N* = 17	Yes SoC *N* = 72	No SoC *N* = 9	No SoC *N* = 1	Yes SoC *N* = 47	Yes SoC *N* = 35	No SoC *N* = 4	Can't Tell *N* = 8	Can't Tell *N* = 60
4. Were the controls selected in an acceptable way?	No No Control Group	Yes 50 Cuff Tear 65 Control	No No Control Group	Yes 6 Control	Yes 7 Control	Yes 120 controls	Yes 19 Control	No No Control Group	No No Control Group	Yes 45 Control	No No Control Group	Can't Tell 10 Control	Can't Tell 60 Control
6. (a) What confounding factors have the authors accounted for?	None Recorded	Gender Age Duration of symptoms Stage of condition Previous Mx	Gender Age Duration of symptoms	Stage of condition	Comorbidities Previous Mx	Gender Age Duration of symptoms Previous Mx Comorbidity	Gender Age Previous Mx	None Recorded	Gender Age Stage of condition Symptom duration	Gender Age	Gender Age Comorbidity Duration of symptoms	Gender Age Comorbidity Duration Of Symptoms	Gender Age Comorbidity Ethnicity Duration of Symptoms
(b) Have the authors taken account of the potential confounding factors in the design and/or in their analysis?	No	Yes Age Comparable Groups - Fs & Rc Tear	No	Yes Stage of condition and Sample	No	Yes Gender affect	Yes Comorbidity Different treatment of Control Group/ "Normals"	No	Yes	No	No	No	Yes
7. Can the results be applied to the local population?	Can't Tell	No Diagnostic Test described awaiting validation	Yes	Can't Tell	No	Yes	No	No	Yes	Can't Tell	No	Can't Tell	Yes
8. Do the results of this study fit with other available evidence?	Can't Tell	Yes	Yes	No	Yes	Yes	No	Can't Tell	Yes	Yes	Yes	Can't Tell	Yes
Overall risk of bias	High	Low	Moderate	Moderate	Moderate	Low	Mod	High	Low	Mod	Moderate	Moderate	Low

Mx management, *SoC* Sample of Convenience, *MRI* Magnetic Resonance Imaging)

Table 5 Inter-operative observations and histological findings

		Bunker [39] Arthroscopy +/− open release *N* = 35	Uhthoff and Boileau [41] Arthroscopy *N* = 4	Xu et al. [37] Arthroscopy *N* = 8
Rotator interval	Appearance	Nodular thickening	No signs of inflammation	----
	Histology	↑ Fibroplasia ↑ Cellularity ↑ Vascularity	↑ Fibroplasia	----
Coraco-humeral ligament	Appearance	----	No signs of inflammation	----
	Histology	----	↑ Fibroplasia ↑ Vascularity	----
Inferior glenohumeral ligament	Appearance	----	No signs of inflammation	----
	Histology	----	----	----
Joint capsule	Appearance	Fibrous contracture in RI area	*Posterosuperior :* No signs of inflammation *Inferior:* No signs of inflammation	*Above subscapularis tendon:* Thickened
	Histology	↑ Vascularity	↑ Fibroplasia ↑ Vascularity	↑ Fibroplasia ↑ Vascularity Neoangiogenesis
Synovium	Appearance	*Between subscapularis bursa and RI:* 4/35 Scarred.	*RI:* Villous *CHL:* No villi *Posterosuperior:* Very villous *Inferior:* No villi *AF:* Very villous	----
	Histology	31/35 Abnormal villous fronding. 31/35 ↑ Vascularity	*RI:* ↑ Vascularity *Posterosuperior:* ↑ Vascularity *AF:* ↑ Vascularity	----
Subscapularis bursa	Appearance	"Consistent abnormalities"	----	----
	Histology	----	----	----
Axillary fold	Appearance	----	No signs of inflammation.	----
	Histology	----	↑ Vascularity	----

N (sample size), ↑ (increased), ↓ (decreased) CHL (coracohumeral ligament), RI (rotator interval), AF (axillary fold), −—(no findings or observations recorded)

evaluates gene expression through the presence of individual cells types, whereas, ICC indicates which proteins those cells are producing [52]. Although they had a relatively small number of participants (*N* = 4) Uhthoff and Boileau [41] conducted a comprehensive study to determine if fibroplasia affects all structures equally. Samples were taken anteriorly, posteriorly, superiorly and inferiorly around the shoulder joint. All structures demonstrated fibroplasia, however, vimentin was strongly expressed anteriorly but was absent in the posterior capsule, leading the authors to suggest that fibroplasia and contracture may be different processes. Their cohort consisted of 4 female subjects with no information pertaining to stage of the condition.

To reduce confounding variables the direct local introduction of medication into the joint was an exclusion criteria for the current review. All patients had failed conservative management; but no studies specified what this included. Common conservative management strategies for FS include oral analgesics and NSAIDs [53]. Therefore, the systemic effects of oral medications should be considered. Evidence in both bone and tendon literature suggests that ibuprofen reduces tensile strength, collagen fibre organisation and fibroblastic proliferation [54]. Almekinders et al. [55] conducted an in-vitro study of the effects of indomethacin on injured human tendon tissue. They reported diminished levels of fibroblast DNA synthesis in the groups treated with

Table 6 Molecular findings

		Bunker [39]	Kilian et al. [33]	Lho et al. [19]	Uhthoff and Boileau [41]	Xu et al. [37]
Techniques used	IHC		X	X	X	X
	ICC	X				
	RTPCR		X	X		
	ELISA			X		
Matrix components	Fibroblasts	↑	↓		↑	
	Myofibroblasts	↑	↓			
Cytokines	IL- 1α			↑		
	IL-1β			↑		
	IL-6			↑		
	TNF-α			↑		
Immune factors	Leukocytes	↓				
	Macrophages	↓				
Neuronal factors	PGP9.5					↑
	GAP43					↑
	P75					↑
Vascular factors	CD34					↑
Enzymes	COX1			↑		
	COX2			↑		

↑ (increased), ↓ (decreased), IHC (immunohistochemistry analysis), ICC (immunocytochemical examination), RTPCR (real time reverse transcription-polymerase chain reaction), ELISA (enzyme-linked immunosorbent assay), IL-1α (interleukin 1 alpha), IL-1β (interleukin 1 beta), IL-6 (interleukin 6), TNF-α (tumour necrosis factor alpha), PGP9.5 (polyclonal rabbit antiprotein gene product 9.5), GAP43 (monoclonal mouse antigrowth-associated protein 43), P75 (nerve growth factor receptor p75), CD34 (monoclonal mouse antihuman CD34), COX1 (cyclooxygenase 1), COX 2 (cyclooxygenase 2)

indomethacin compared to control. It is important to acknowledge that levels of reported fibroplasia may have been influenced by pharmaceutical preparations potentially prescribed to treat the symptoms.

Inflammation and immune modulation

Cyclooxygenases play an important role in inflammation and the collagen catabolic process within peripheral tissues [53]. Lho et al. [19] used RTPCR and IHC and reported increased expression of COX1 in the endothelial cells and stroma of the joint capsule and increased expression of COX2 in the capsule and subacromial bursa of the FS group. Furthermore, levels of IL-1α, IL-β, IL6 and TNF-α also differed between the capsule, bursa and joint fluid. Interleukin and TNF-α are pro-inflammatory cytokines; released from immune cells such as macrophages [54]. This may imply that high numbers of these cells may be present in the joint [56]. Bunker [39] reported low numbers of macrophages and leukocytes in the RI. This variation may be reflective of differing pathological processes between structures and/or that the biopsies were taken from different stages of disease, and possibly different diagnostic criteria. Neither Bunker [39] nor Lho et al. [19] provided sufficient background data regarding their participants to explore this. Furthermore, no comparable studies were included in this SR which again reveals a gap in the evidence base that is worthy of exploration.

Neuronal and vascular factors

Pain is associated with FS [3]. Hand et al. [6] conducted a longitudinal study of 223 patients with frozen shoulder with a mean follow up time of 4.4 years (range 2 to 20 years), with 41 % of the patient's reporting mild to moderate pain and 6 % reported severe pain. To date, few studies have investigated the causes of pain experienced by patients with FS [57]. In this review, Xu et al. [37] investigated neuronal components associated with PFS, reporting elevated levels of several immunoreactive neuronal proteins (GAP43, PGP9.5 and P75) in the anterosuperior joint capsule, close to small blood vessels or within fibroblastic tissue. These findings confirm the presence of mature and regenerating nerve fibres in the anterosuperior capsule and may explain the severe pain experienced by sufferers of the condition in the early stages (less than six months). Increased vascularity was a common feature identified in the histology studies; particularly located in the anterosuperior structures but absent in the inferior structures (with the exception of the axillary fold (AF)). This is consistent with the literature where hypervascularity and angiogenesis have been reported as potential sources of pain due to their

association with neovessels [58, 59]. Xu et al. [37] reported stronger expression of CD34 (a haematopoietic cell marker) in the superior joint capsule of the FS group compared RC tears, as a control population. Limited conclusions may be drawn from this study because of the small sample size (n = 8). Ryu et al. [58] investigated FS in a diabetic cohort and reported CD34 to be strongly expressed. However, caution must be taken when extrapolating these results as the patient's had received corticosteroid injections. A recent study by Okuno et al. [59] reported that arterial embolization of neovessels in the RI provided rapid relief of pain in their FS group. Limited knowledge exists regarding the pain mechanisms involved with FS [60]. This SR has provided some insight into possible causes. This knowledge has great significance for clinicians as pain is often the dominant complaint in patients with FS. The literature has suggested that the condition may manifest differently between individuals. A greater understanding would greatly assist clinicians to effectively manage this symptom in their patients. It is clear further research is required.

Limitations

It is acknowledged that this systematic review has a number of limitations. These are reviewed in the following section.

Searches

Only English language publications were included in this review so the introduction of language bias cannot be ruled out. Studies where an English translation could not be sourced were identified during abstract analysis. One reviewer (VR) identified eighteen studies where the full text English article could not be sourced. The second reviewer (HB) identified six of those eighteen. All eighteen studies were excluded. The evidence surrounding language bias is conflicting [30], and it is not known how these non-English publications may have influenced the findings of the current review.

No date restriction was applied to the studies so that all available studies could be identified and included in this systematic review, believed to be the first of this type, in this condition. MRI was first introduced into healthcare in the 1980's, and over time image quality has advanced substantially [61]. The implication of this is that the reported imaging findings from the earlier studies [32, 35] may lack the sensitivity of those in later studies [31]. This also may have influenced the findings and contributed to reported discrepancies.

Inclusion and exclusion criteria

The aim of the review was to investigate the intra and peri-articular pathophysiology of the glenohumeral joint in people diagnosed with primary idiopathic frozen shoulder. Only studies specifying primary frozen shoulder were included as it was not possible to separate the findings from investigations that included both primary and secondary frozen shoulders. This meant that primary frozen shoulder findings may have been missed by excluding studies that incorporated both. The decision to only include samples from people diagnosed with primary FS hopefully generated more homogenised data.

Direct injection of medication into the joint was an exclusion criteria in this review to reduce the potential confounding influencing this may have had on the findings. However, there may be other sources of confounding which might have affected the findings of this review. All patients included in the review had had failed conservative management but none of the studies specified what this included. Common conservative management strategies for frozen shoulder include oral analgesics and NSAIDs [62] and potentially, the systemic effects of such oral medications may have also influenced findings.

Widespread variation

The main limitation of this review relates to the included studies. Variations in diagnosis, methods of sample selection, timing of sampling, and confounding variables such as use of oral medications, all may have influenced the reported findings and the conclusions of this review. Meta-analysis was not considered due to the considerable and widespread variance within the included studies [30].

Risk of bias

The majority of studies (n = 7) were identified as having a moderate risk of bias, with two studies assessed of being at high risk of bias and the remaining four rated as low risk of bias. Study characteristics were poorly reported. There are three possible concerns for this review. The first is, as previously mentioned, a risk of bias tool specifically for use in pathophysiology reviews was not found, meaning there may be specific domains relevant for this type of review which have not been appraised or discussed. The second is that, with only a minority of studies being assessed as low risk of bias, the findings of this review may contain systematic bias [30]. Meta-analyses were not included in this review: it is accepted that meta-analyses of studies that are at risk of bias may be seriously misleading since meta-analysis may simply compound the errors, thus producing an erroneous results which may be interpreted as having more credibility [30]. The third concern is that the ACROBAT-NRSI tool, as a recent development to meet the need for a tool to assess risk of bias in non-randomised studies, has yet to be widely used or evaluated. Further research on the performance of the tool in the future may influence the

findings of this review or enable the findings to be placed more appropriately in context.

Conclusions

This systematic review is the first review to synthesise imaging and histological studies to examine the pathophysiology associated with primary frozen shoulder. The review highlights the role of the anterior shoulder structures in primary frozen shoulder, but there is a lack of available evidence considered at low risk of bias to inform understanding of the pathophysiology of the primary frozen shoulder condition. Consensus regarding inclusion criteria (and the interpretation of the Codman classification criteria) is first required for future research to promote studies providing comparable findings. Following this, further studies that identify findings at clearly defined stages of the condition are required to improve the understanding of the disease continuum. Improved understanding may then inform management specific to each stage of this painful, disabling common condition so that it is no longer difficult to define, treat or explain.

Abbreviations

ACROBAT-NRSI, a cochrane risk of bias assessment tool for non-randomized studies of interventions; AF, axillary fold; AMED, allied and complementary medicine database; BNI, British nursing index; CHL, coracohumeral ligament; CINAHL, cumulative index to nursing and allied health literature; FS, frozen shoulder; ICC, immunocytochemistry; IHC, immunohistochemistry; IL, interleukin; LHB, long head of biceps; MRA, magnetic resonance angiogram; MRI, magnetic resonance imaging; mRNA, messenger RNA; MUA, manipulation under anaesthetic; NSAIDs, non-steroidal anti-inflammatory drugs; PFS, primary frozen shoulder; PICO, population, intervention, comparator and outcome; PRISMA, preferred reporting items for systematic reviews and meta-analyses; QUADAS-2, quality assessment of diagnostic accuracy studies; RTPCR, reverse transcription polymerase chain reaction; TNF, tumour necrosis factor

Competing interests

The authors declare that they have no competing interests.

References

1. Kelley MJ, Shaffer MA, Kuhn JE, Michener LA, Seitz AL, Uhl TL, et al. Shoulder pain and mobility deficits: adhesive capsulitis. J Orthop Sports Phys Ther. 2013;43(5):A1–31. doi:10.2519/jospt.2013.0302. 10.2519/jospt.2013.43.1.A1.
2. Lewis J. Frozen shoulder contracture syndrome - Aetiology, diagnosis and management. Man Ther. 2015;20(1):2–9. doi:10.1016/j.math.2014.07.006.
3. Jones S, Hanchard N, Hamilton S, Rangan A. A qualitative study of patients' perceptions and priorities when living with primary frozen shoulder. BMJ open. 2013;3(9):e003452. doi:10.1136/bmjopen-2013-003452.
4. Reeves B. The natural history of the frozen shoulder syndrome. Scand J Rheumatol. 1975;4(4):193–6.
5. Shaffer B, Tibone JE, Kerlan RK. Frozen shoulder. A long-term follow-up. J Bone Joint Surg. 1992;74(5):738–46.
6. Hand C, Clipsham K, Rees JL, Carr AJ, et al. Long-term outcome of frozen shoulder. J Shoulder Elbow Surgery. 2008;17(2):231–6. doi:10.1016/j.jse.2007.05.009.
7. Urwin M, Symmons D, Allison T, Brammah T, Busby H, Roxby M, et al. Estimating the burden of musculoskeletal disorders in the community: the comparative prevalence of symptoms at different anatomical sites, and the relation to social deprivation. Ann Rheum Dis. 1998;57(11):649–55.
8. Codman E. The Shoulder: Rupture of the supraspinatus tendon and other lesions in or about the subacromial bursa. Boston: Thomas Todd Company; 1934.
9. Lundberg BJ. The frozen shoulder. Acta Orthop Scand Suppl. 1969;119:1–59.
10. Zuckerman JD, Coumo F, Rokito S. Definition and classification of frozen shoulder: A consensus approach. Journal of Shoulder and Elbow Surgery. 1994;3(S72).
11. Hand GC, Athanasou NA, Matthews T, Carr AJ. The pathology of frozen shoulder. J Bone Joint Surg. 2007;89(7):928–32. doi:10.1302/0301-620X.89B7.19097.
12. Zuckerman JD, Rokito A, et al. Frozen shoulder: a consensus definition. J Shoulder Elbow Surgery. 2011;20(2):322–5. doi:10.1016/j.jse.2010.07.008.
13. Milgrom C, Novack V, Weil Y, Jaber S, Radeva-Petrova DR, Finestone A. Risk factors for idiopathic frozen shoulder. Israel Med Assoc J. 2008;10(5):361–4.
14. Sofka CM, Ciavarra GA, Hannafin JA, Cordasco FA, Potter HG. Magnetic resonance imaging of adhesive capsulitis: correlation with clinical staging. HSS J. 2008;4(2):164–9. doi:10.1007/s11420-008-9088-1.
15. Tamai K, Akutsu M, Yano Y. Primary frozen shoulder: brief review of pathology and imaging abnormalities. J Orthopaedic Sci. 2014;19(1):1–5. doi:10.1007/s00776-013-0495-x.
16. Duplay S. De la periarthrite scapulo-humerale. Rev frat d trav de med. 1896;53:226.

17. Neviaser J. Adhesive capsulitis of the shoulder. A study of the pathological findings in periarthritis of the shoulder. J Bone Joint Surgery (Am). 1945;27(2):211–22.
18. Gondim Teixeira PA, Balaj C, Chanson A, Lecocq S, Louis M, Blum A. Adhesive capsulitis of the shoulder: value of inferior glenohumeral ligament signal changes on T2-weighted fat-saturated images. AJR Am J Roentgenol. 2012;198(6):W589–96. doi:10.2214/AJR.11.7453.
19. Lho YM, Ha E, Cho CH, Song KS, Min BW, Bae KC, et al. Inflammatory cytokines are overexpressed in the subacromial bursa of frozen shoulder. J Shoulder Elbow Surgery. 2013;22(5):666–72. doi:10.1016/j.jse.2012.06.014.
20. Bunker TD, Reilly J, Baird KS, Hamblen DL. Expression of growth factors, cytokines and matrix metalloproteinases in frozen shoulder. J Bone Joint Surg. 2000;82(5):768–73.
21. Bunker TD, Anthony PP. The pathology of frozen shoulder. A Dupuytren-like disease. J Bone Joint Surg. 1995;77(5):677–83.
22. Omari A, Bunker TD, et al. Open surgical release for frozen shoulder: surgical findings and results of the release. J Shoulder Elbow Surgery. 2001;10(4):353–7.
23. Kanbe K, Inoue K, Inoue Y, Chen Q. Inducement of mitogen-activated protein kinases in frozen shoulders. J Orthopaedic Sci. 2009;14(1):56–61. doi:10.1007/s00776-008-1295-6.
24. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009; 339:b2535. doi:10.1136/bmj.b2535.
25. Sackett D, Straus S, Richardson W, Rosenberg W, Haynes R. Evidence-based medicine. How to teach and practice EBM. 2 ed. Edinburgh: Churchill Livingstone; 2000.
26. Dean BJ, Lostis E, Oakley T, Rombach I, Morrey ME, Carr AJ. The risks and benefits of glucocorticoid treatment for tendinopathy: a systematic review of the effects of local glucocorticoid on tendon. Semin Arthritis Rheum. 2014;43(4):570–6. doi:10.1016/j.semarthrit.2013.08.006.
27. Favejee MM, Huisstede BM, Koes BW. Frozen shoulder: the effectiveness of conservative and surgical interventions–systematic review. Br J Sports Med. 2011;45(1):49–56. doi:10.1136/bjsm.2010.071431.
28. Loew M, Heichel TO, Lehner B, et al. Intraarticular lesions in primary frozen shoulder after manipulation under general anesthesia. J Shoulder Elbow Surgery. 2005;14(1):16–21. doi:10.1016/j.jse.2004.04.004.
29. UoYCfRa D. Systematic reviews: CRD's guidance for undertaking reviews in health care. York: York Publishing Services Ltd.; 2009.
30. Higgins JP. Cochrane handbook for systematic reviews of interventions (Vol. 5). Chichester: Wiley-Blackwell; 2008.
31. Carbone S, Napoli A, Gumina S. MRI of adhesive capsulitis of the shoulder: distension of the bursa in the superior subscapularis recess is a suggestive sign of the pathology. Eur J Radiol. 2014;83(2):345–8. doi:10.1016/j.ejrad.2013.10.017.
32. Carrillon Y, Noel E, Fantino O, Perrin-Fayolle O, Tran-Minh VA. Magnetic resonance imaging findings in idiopathic adhesive capsulitis of the shoulder. Rev Rhum Engl Ed. 1999;66(4):201–6.
33. Kilian O, Pfeil U, Wenisch S, Heiss C, Kraus R, Schnettler R. Enhanced alpha 1(I) mRNA expression in frozen shoulder and dupuytren tissue. Eur J Med Res. 2007;12(12):585–90.
34. Li JQ, Tang KL, Wang J, Li QY, Xu HT, Yang HF, et al. MRI findings for frozen shoulder evaluation: is the thickness of the coracohumeral ligament a valuable diagnostic tool? PLoS One. 2011;6(12):e28704. doi:10.1371/journal.pone.0028704.
35. Manton GL, Schweitzer ME, Weishaupt D, Karasick D. Utility of MR arthrography in the diagnosis of adhesive capsulitis. Skeletal Radiol. 2001;30(6):326–30.
36. Song KD, Kwon JW, Yoon YC, Choi SH. Indirect MR arthrographic findings of adhesive capsulitis. AJR Am J Roentgenol. 2011;197(6):W1105–9. doi:10.2214/AJR.10.6099.
37. Xu Y, Bonar F, Murrell GA, et al. Enhanced expression of neuronal proteins in idiopathic frozen shoulder. J Shoulder Elbow Surgery. 2012;21(10):1391–7. doi:10.1016/j.jse.2011.08.046.
38. Zhao W, Zheng X, Liu Y, Yang W, Amirbekian V, Diaz LE, et al. An MRI study of symptomatic adhesive capsulitis. PLoS One. 2012;7(10):e47277. doi:10.1371/journal.pone.0047277.
39. Bunker TD. Frozen shoulder: unravelling the enigma. Ann R Coll Surg Engl. 1997;79(3):210–3.
40. Neviaser JS. Arthrography of the shoulder joint: study of the findings in adhesive capsulitis of the shoulder. Study of the findings in adhesive capsulitis of the shoulder. J Bone Joint Surgery. 1962;44-A:1321–59.
41. Uhthoff HK, Boileau P. Primary frozen shoulder: global capsular stiffness versus localized contracture. Clin Orthop Relat Res. 2007;456:79–84. doi:10.1097/BLO.0b013e318030846d.
42. Xu Y, Bonar F, Murrell GA. Enhanced expression of neuronal proteins in idiopathic frozen shoulder. Journal of shoulder and elbow surgery / American Shoulder and Elbow Surgeons. 2011
43. Chundru U, Riley GM, Steinbach LS. Magnetic resonance arthrography. Radiol Clin North Am. 2009;47(3):471–94. doi:10.1016/j.rcl.2009.02.001.
44. Elentuck D, Palmer WE. Direct magnetic resonance arthrography. Eur Radiol. 2004;14(11):1956–67. doi:10.1007/s00330-004-2449-3.
45. Emig EW, Schweitzer ME, Karasick D, Lubowitz J. Adhesive capsulitis of the shoulder: MR diagnosis. AJR Am J Roentgenol. 1995;164(6):1457–9. doi:10.2214/ajr.164.6.7754892.
46. Kim KC, Rhee KJ, Shin HD, et al. Adhesive capsulitis of the shoulder: dimensions of the rotator interval measured with magnetic resonance arthrography. J Shoulder Elbow Surgery. 2009;18(3):437–42. doi:10.1016/j.jse.2008.10.018.
47. Mengiardi B, Pfirrmann CW, Gerber C, Hodler J, Zanetti M. Frozen shoulder: MR arthrographic findings. Radiology. 2004;233(2):486–92. doi:10.1148/radiol.2332031219.
48. Bergin D, Schweitzer ME. Indirect magnetic resonance arthrography. Skeletal Radiol. 2003;32(10):551–8. doi:10.1007/s00256-003-0669-2.
49. Ozaki J, Nakagawa Y, Sakurai G, Tamai S. Recalcitrant chronic adhesive capsulitis of the shoulder. Role of contracture of the coracohumeral ligament and rotator interval in pathogenesis and treatment. J Bone Joint Surgery. 1989;71(10):1511–5.
50. Rodeo SA, Hannafin JA, Tom J, Warren RF, Wickiewicz TL. Immunolocalization of cytokines and their receptors in adhesive capsulitis of the shoulder. J Orthopaedic Res. 1997;15(3):427–36. doi:10.1002/jor.1100150316.
51. Smith SP, Devaraj VS, Bunker TD, et al. The association between frozen shoulder and Dupuytren's disease. J Shoulder Elbow Surgery. 2001;10(2):149–51.
52. Dean BJ, Franklin SL, Carr AJ. A systematic review of the histological and molecular changes in rotator cuff disease. Bone Joint Res. 2012;1(7):158–66. doi:10.1302/2046-3758.17.2000115.
53. Dyson M. Inflammation, wounds and wound healing. In: Shamley D, editor. Pathophysiology. Edinburgh: Elsevier; 2005. p. 3–15.
54. Shahriari S, Rezaei A, Jalalzadeh SM, Mani K, Zamani A. Effect of Ibuprofen on IL-1beta, TNF-alpha and PGE2 levels in periapical exudates: a double blinded clinical trial. Iran J Immunol. 2011;8(3):176–82. IJIv8i3A5.
55. Almekinders LC, Baynes AJ, Bracey LW. An in vitro investigation into the effects of repetitive motion and nonsteroidal antiinflammatory medication on human tendon fibroblasts. Am J Sports Med. 1995;23(1):119–23.
56. Shamley D. Diseases of the immune system. In: Shamley D, editor. Pathophysiology. Edinburgh: Elsevier; 2005. p. 3–15.
57. Ochiai N, Ohtori S, Kenmoku T, Yamazaki H, Ochiai S, Saisu T, et al. Sensory innervation of rat contracture shoulder model. J Shoulder Elbow Surgery. 2013;22(2):158–64. doi:10.1016/j.jse.2012.02.011.
58. Ryu JD, Kirpalani PA, Kim JM, Nam KH, Han CW, Han SH, et al. Expression of vascular endothelial growth factor and angiogenesis in the diabetic frozen shoulder. J Shoulder Elbow Surgery. 2006;15(6):679–85. doi:10.1016/j.jse.2006.01.002.
59. Okuno Y, Oguro S, Iwamoto W, Miyamoto T, Ikegami H, Matsumura N, et al. Short-term results of transcatheter arterial embolization for abnormal neovessels in patients with adhesive capsulitis: a pilot study. J Shoulder Elbow Surgery. 2014;23(9):e199–206. doi:10.1016/j.jse.2013.12.014.
60. Dawson J, Shepperd S, Carr A. An overview of factors relevant to undertaking research and reviews on the effectiveness of treatment for frozen shoulder. Shoulder Elbow. 2010;2:232–7.
61. Sobol WT. Recent advances in MRI technology: Implications for image quality and patient safety. Saudi J Ophthalmol. 2012;26(4):393–9. doi:10.1016/j.sjopt.2012.07.005.
62. Hsu JE, Anakwenze OA, Warrender WJ, Abboud JA, et al. Current review of adhesive capsulitis. J Shoulder Elbow Surgery. 2011;20(3):502–14. doi:10.1016/j.jse.2010.08.023.

Left and Non-Dominant Shoulders Were More Frequently Affected in Patients with Frozen Shoulder: A Systematic Review and Meta-Analysis

Abstract

Background: If trauma has a considerable impact on frozen shoulder, the right or dominant shoulder is more frequently affected than the left or non-dominant shoulder. Herein it is examined whether the right or dominant shoulder was more frequently affected in patients with frozen shoulder using PubMed.

Materials and methods: PubMed was searched to retrieve relevant studies. The search term used was frozen shoulder. The studies obtained were published between 1966 and 2007, and included 10 or more patients with only one affected side. Patients with bilateral shoulder involvement were excluded.

Results: The right shoulder was affected in 718 patients (46.3%), while the left shoulder was affected in 833 (53.7%). The dominant shoulder was affected in 298 patients (41.1%), while the non-dominant shoulder was affected in 427 (58.9%). The left shoulder was affected significantly more than the right shoulder ($p<0.01$). The non-dominant shoulder was affected significantly more than the dominant shoulder ($p<0.01$).

Conclusion: Trauma including repeated minor trauma is less likely to cause frozen shoulder, or the influence of brain abnormalities is stronger than that of trauma. The left shoulder may have been more frequently affected because of the side-to-side asymmetry of the brain for various reasons. If this hypothesis is correct, brain abnormalities may be one cause of frozen shoulder, suggesting that central neuropathic pain or braingenic pain contributes to the pain associated with frozen shoulder. The right and dominant shoulders were less frequently affected in patients with frozen shoulder.

Keywords: Frozen shoulder; Side-to-side asymmetry; Dominant hand; Right; Left; Frequency

Introduction

Trauma including repeated minor trauma may cause frozen shoulder [1]. If trauma has a considerable impact on frozen shoulder, the right or dominant shoulder is more frequently affected than the left or non-dominant shoulder. Herein it is examined whether the right or dominant shoulder was more frequently affected using PubMed.

Materials and Methods

PubMed was searched to retrieve relevant studies. The search term used was "frozen shoulder." The following inclusion criteria were employed; (1) Studies published between 1966 and 2007; (2) Studies written in English; (3) Studies including 10 or more patients with only one affected side. Patients with bilateral shoulder involvement were excluded; (4) Studies comprising full reports (no letters or abstracts); (5) If one group published 2 or more studies, only one study with the largest number of patients was used; (6) The study by Weiser [2] reported the following: the left and right side were equally involved (n=100). The study by Bunker et al. [3] demonstrated that "The left and right shoulders were equally involved (n=50). Therefore, the right side is considered to be involved in 50% of patients in these studies [2,3] (Figure 1). The goodness-of-fit test was applied. A P value<0.01 was considered to be significant.

Results

The right shoulder was affected in 718 patients (46.3%), while the left shoulder was affected in 833 (53.7%). The dominant shoulder was affected in 298 patients (41.1%), while the non-dominant shoulder was affected in 427 (58.9%). The left shoulder was affected significantly more than the right shoulder ($p<0.01$). The non-dominant shoulder was affected significantly more than the dominant shoulder ($p<0.01$) (Table 1).

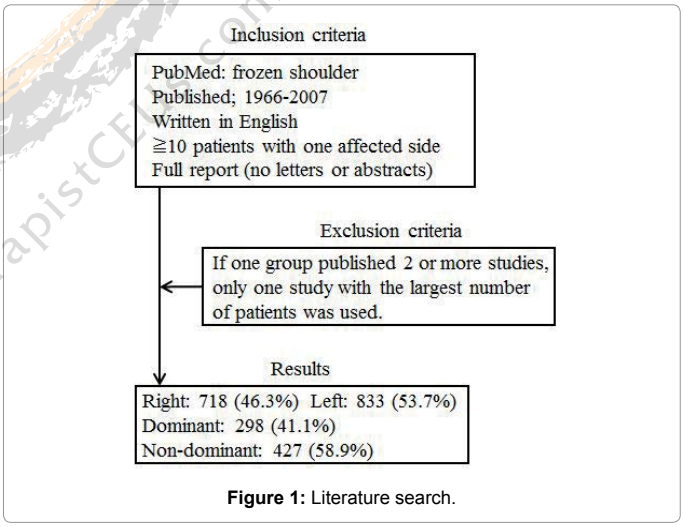

Figure 1: Literature search.

Discussion

The cause of frozen shoulder currently remains unknown. A systematic review showed that the pathophysiology associated with

***Corresponding author:** Dr. Katsuhiro Toda, Department of Orthopedic Surgery, Kitahiroshima Town Toyohira Hospital, 4705, Azaka, Kita-Hriroshima Town, Yamagata-Gun, Hiroshima, 731-1222, Japan, Tel: +81-826-84-1155; E-mail: goutattack@yahoo.co.jp

Received June 01, 2018 ; **Accepted** June 28, 2018; **Published** July 05, 2018

Citation: Toda K (2018) Left and Non-Dominant Shoulders Were More Frequently Affected in Patients with Frozen Shoulder: A Systematic Review and Meta-Analysis. Orthop Muscular Syst 7: 258. doi:10.4172/2161-0533.1000258

Year	Author	Right	Left	Sum	Dominant	Non-dominant	Sum	Number of articles
1969	Lundberg	90	142	232				8
1975	Reeves	23	17	40				9
1977	Weiser	50	50	100				2
1983	Helbig	70	44	114				10
1984	Bulgen				22	19	41	11
1989	Parker	13	11	24	15	9	24	12
1991	Hsu	20	55	75				13
1993	Uitvlugt	7	12	19	7	12	19	14
1995	Bunker	25	25	50				3
1995	Weber	16	22	38	13	20	33	15
1995	Melzer	56	52	108				16
1998	Gam	49	45	94				17
1998	Leppala				18	35	53	18
1999	Reichmister	10	16	26	10	16	26	19
1999	O'Kane	12	24	36				20
1999	Okamura	21	9	30				21
2000	Watson	36	31	67				22
2000	Dodenhoff	16	19	35	24	11	35	23
2001	Carter	11	9	20	9	11	20	24
2001	Omari	13	12	25				25
2002	Klinger	19	17	36				26
2002	Vermeulen	7	3	10				27
2002	Massoud	18	21	39	18	21	39	28
2002	Halverson	11	10	21				29
2002	Othman				22	32	54	30
2003	Hamdan	29	61	90	24	66	90	31
2003	Rundquist	4	6	10				32
2004	Buchbinder	23	26	49				33
2004	Widiastuti-Samekto	11	16	27				34
2005	Khan	23	12	35				35
2006	Ma				33	42	75	36
2006	Ryu	4	6	10				37
2007	Kivimaki	42	83	125	41	84	125	38
2007	Amir-Us-Saqlain	9	24	33	9	24	33	39
2007	Baums	18	12	30	18	12	30	40
2007	Sakeni	52	83	135				41
2007	Yang				15	13	28	42
	Total	718	833	1551	298	427	725	

Table 1: Results of shoulder affected patients.

primary (idiopathic) frozen shoulder was inconclusive [4]. Trauma including repeated minor trauma may cause frozen shoulder [1]. If this hypothesis is correct, the right or dominant shoulder is more frequently affected. However, in contrast to predictions, the left and non-dominant shoulders were more frequently affected. Trauma including repeated minor trauma may be less likely to cause frozen shoulder, while the influence of brain abnormalities appears to be stronger than that of trauma.

It currently remains unclear why the left and non-dominant shoulders are more frequently affected. Based on previous findings, Merskey et al. reported that pain was more often lateralized on the left, except in the case of trigeminal neuralgia [5]. Previous experimental evidence implied that the right hemisphere was less efficient than the left in processing cutaneous sensory input [5]. Ertunc et al. reported that the herpes zoster infection frequency was higher in right-handed patients and more frequently appeared in the left body side of females [6]. Dane et al. showed that the cell-mediated hypersensitivity was stronger in the left side of the body than the right based on the tuberculin test with 22 male and 36 female healthy high school students [7]. The left shoulder may have been more frequently affected by frozen shoulder because of the side-to-side asymmetry of the brain for various reasons. If this hypothesis is correct, brain abnormalities are one of the causes of frozen shoulder, suggesting that central neuropathic pain or braingenic pain contributes to the pain associated with frozen shoulder.

The non-dominant shoulder (58.9%) was more frequently affected than the left shoulder (53.7%). The reason for this remains unknown. It may be due to the roles of the right brain in right-handedness and those of the left brain in left-handedness not necessarily being the same, as well as the roles of the right brain in left-handedness and those of the left brain in right-handedness not necessarily being the same [2,3,8-42].

Limitations

Some physicians may believe that trauma including repeated minor trauma causes frozen shoulder. These physicians may be more likely to think that the right or dominant shoulder is more frequently affected than the left or non-dominant shoulder. Therefore, in case that the left or non-dominant shoulder is more frequently affected than the right or

dominant shoulder, it is possible that they are more likely to interested in it and report it. These may cause a bias.

Conclusion

The right shoulder was affected in 718 patients (46.3%), while the left shoulder was affected in 833 (53.7%). The dominant shoulder was affected in 298 patients (41.1%), while the non-dominant shoulder was affected in 427 (58.9%). The left shoulder was affected significantly more than the right shoulder ($p<0.01$). The non-dominant shoulder was affected significantly more than the dominant shoulder ($p<0.01$).

Conflict of Interest

The author confirms that this article content has no conflict of interest.

Acknowledgement

I thank Medical English Service for reviewing this manuscript.

References

1. Harryman DT, 2nd (1993) Shoulders: Frozen and stiff. Instr Course Lect 42: 247-257.
2. Weiser HI (1977) Painful primary frozen shoulder mobilization under local anesthesia. Arch Phys Med Rehabil 58: 406-408.
3. Bunker TD, Anthony PP (1995) The pathology of frozen shoulder. A Dupuytren-like disease. J Bone Joint Surg Br 77: 677-683.
4. Ryan V, Brown H, Minns Lowe CJ, Lewis JS (2016) The pathophysiology associated with primary (idiopathic) frozen shoulder: A systematic review. BMC Musculoskelet Disord 17: 340.
5. Merskey H, Watson GD (1979) The lateralisation of pain. Pain 7: 271-280.
6. Ertunc V, Dane S, Karakuzu A, Deniz O (1997) Higher herpes zoster infection frequency in right-handed patients and more frequent appearance in the left body side of females. Acta Derm Venereol 77: 245.
7. Dane S, Erdem T, Gumustekin K (2001) Cell-mediated immune hypersensitivity is stronger in the left side of the body than the right in healthy young subjects. Percept Mot Skills 93: 329-332.
8. Lundberg BJ (1969) The frozen shoulder: Clinical and radiographical observations. The effect of manipulation under general anesthesia, structure and glycosaminoglycan content of the joint capsule, local bone metabolism. Acta Orthop Scand Suppl 119: 1-59.
9. Reeves B (1975) The natural history of the frozen shoulder syndrome. Scand J Rheumatol 4: 193-196.
10. Helbig B, Wagner P, Dohler R (1983) Mobilization of frozen shoulder under general anaesthesia. Acta Orthop Belg 49: 267-274.
11. Bulgen DY, Binder AI, Hazleman BL, Dutton J, Roberts S (1984) Frozen shoulder: Prospective clinical study with an evaluation of three treatment regimens. Ann Rheum Dis 43: 353-360.
12. Parker RD, Froimson AI, Winsberg DD, Arsham NZ (1989) Frozen shoulder. Part II: Treatment by manipulation under anesthesia. Orthopedics 12: 989-990.
13. Hsu SY, Chan KM (1991) Arthroscopic distension in the management of frozen shoulder. Int Orthop 15: 79-83.
14. Uitvlugt G, Detrisac DA, Johnson LL, Austin MD, Johnson C (1993) Arthroscopic observations before and after manipulation of frozen shoulder. Arthroscopy 9: 181-185.
15. Weber M, Prim J, Bugglin R, Michel BA, Gerber H (1995) Long-term follow up to patients with frozen shoulder after mobilization under anesthesia, with special reference to the rotator cuff. Clin Rheumatol 14: 686-691.
16. Melzer C, Wallny T, Wirth CJ, Hoffman S (1995) Frozen shoulders- treatment and results. Arch Orthop Trauma Surg 114: 87-91.
17. Gam AN, Schydlowsky P, Rossel I, Remvig L, Jensen EM (1998) Treatment of "frozen shoulder" with distension and glucorticoid compared with glucorticoid alone. A randomised controlled trial. Scand J Rheumatol 27: 425-430.
18. Leppala J, Kannus P, Sievanen H, Jarvinen M, Vuori I (1998) Adhesive capsulitis of the shoulder (frozen shoulder) produces bone loss in the affected humerus, but long-term bony recovery is good. Bone 22: 691-694.
19. Reichmister JP, Friedman SL (1999) Long-term functional results after manipulation of the frozen shoulder. Md Med J 48: 7-11.
20. O'Kane JW, Jackins S, Sidles JA, Smith KL, Matsen FA (1999) Simple home program for frozen shoulder to improve patients' assessment of shoulder function and health status. J Am Board Fam Pract 12: 270-277.
21. Okamura K,Ozaki J (1999) Bone mineral density of the shoulder joint in frozen shoulder. Arch Orthop Trauma Surg 119: 363-367.
22. Watson L, Dalziel R, Story I (2000) Frozen shoulder: A 12-month clinical outcome trial. J Shoulder Elbow Surg 9: 16-22.
23. Dodenhoff RM, Levy O, Wilson A, Copeland SA (2000) Manipulation under anesthesia for primary frozen shoulder: effect on early recovery and return to activity. J Shoulder Elbow Surg 9: 23-26.
24. Carter B (2001) A pilot study to evaluate the effectiveness of Bowen technique in the management of clients with frozen shoulder. Complement Ther Med 9: 208-215.
25. Omari A, Bunker TD (2001) Open surgical release for frozen shoulder: Surgical findings and results of the release. J Shoulder Elbow Surg 10: 353-357.
26. Klinger HM, Otte S, Baums MH, Haerer T (2002) Early arthroscopic release in refractory shoulder stiffness. Arch Orthop Trauma Surg 122: 200-203.
27. Vermeulen HM, Stokdijk M, Eilers PH, Meskers CG, Rozing PM, et al. (2002) Measurement of three dimensional shoulder movement patterns with an electromagnetic tracking device in patients with a frozen shoulder. Ann Rheum Dis 61: 115-120.
28. Massoud SN, Pearse EO, Levy O, Copeland SA (2002) Operative management of the frozen shoulder in patients with diabetes. J Shoulder Elbow Surg 11: 609-613.
29. Halverson L,Maas R (2002) Shoulder joint capsule distension (hydroplasty): A case series of patients with "frozen shoulders" treated in a primary care office. J Fam Pract 51: 61-63.
30. Othman A,Taylor G (2002) Manipulation under anaesthesia for frozen shoulder. Int Orthop 26: 268-270.
31. Hamdan TA, Al-Essa KA (2003) Manipulation under anaesthesia for the treatment of frozen shoulder. Int Orthop 27: 107-109.
32. Rundquist PJ, Anderson DD, Guanche CA, Ludewig PM (2003) Shoulder kinematics in subjects with frozen shoulder. Arch Phys Med Rehabil 84: 1473-1479.
33. Buchbinder R, Hoving JL, Green S, Hall S, Forbes A, et al. (2004) Short course prednisolone for adhesive capsulitis (frozen shoulder or stiff painful shoulder): A randomised, double blind, placebo controlled trial. Ann Rheum Dis 63: 1460-1469.
34. Widiastuti-Samekto M, Sianturi GP (2004) Frozen shoulder syndrome: Comparison of oral route corticosteroid and intra-articular corticosteroid injection. Med J Malaysia 59: 312-316.
35. Khan AA, Mowla A, Shakoor MA, Rahman MR (2005) Arthrographic distension of the shoulder joint in the management of frozen shoulder. Mymensingh Med J 14: 67-70.
36. Ma T, Kao MJ, Lin IH, Chiu YL, Chien C, et al. (2006) A study on the clinical effects of physical therapy and acupuncture to treat spontaneous frozen shoulder. Am J Chin Med 34: 759-775.
37. Ryu JD, Kirpalani PA, Kim JM, Nam KH, Han CW, et al. (2006) Expression of vascular endothelial growth factor and angiogenesis in the diabetic frozen shoulder. J Shoulder Elbow Surg 15: 679-685.
38. Kivimaki J, Pohjolainen T, Malmivaara A, Kannisto M, Guillaume J, et al. (2007) Manipulation under anesthesia with home exercises versus home exercises alone in the treatment of frozen shoulder: A randomized, controlled trial with 125 patients. J Shoulder Elbow Surg 16: 722-726.
39. Amir-Us-Saqlain H, Zubairi A, Taufiq I (2007) Functional outcome of frozen shoulder after manipulation under anaesthesia. J Pak Med Assoc 57: 181-185.
40. Baums MH, Spahn G, Nozaki M, Steckel H, Schultz W, et al. (2007) Functional outcome and general health status in patients after arthroscopic release in adhesive capsulitis. Knee Surg Sports Traumatol Arthrosc 15: 638-644.
41. Sakeni RA, Al-Nimer MS (2007) Comparison between intra-articular triamcinolone acetonide and methylprednisolone acetate injections in treatment of frozen shoulder. Saudi Med J 28: 707-712.
42. Yang JL, Chang CW, Chen SY, Wang SF, Lin JJ (2007) Mobilization techniques in subjects with frozen shoulder syndrome: Randomized multiple-treatment trial. Phys Ther 87: 1307-1315.

Shoulder proprioception – lessons we learned from idiopathic frozen shoulder

Abstract

Background: Of all the most frequent soft tissue disorders of the shoulder, idiopathic frozen shoulder (IFS) offers the greatest potential for studying proprioception. Studies concerning the presence of proprioception dysfunctions have failed to determine the potential for spontaneous healing of passive shoulder stabilizers (anterior and posterior capsule, middle and inferior gleno-humeral ligaments), its relationship with passive (PJPS) and active (AJPS) shoulder proprioception for internal and external rotation (IR, ER), as well as the isokinetic muscle performance of the internal and external rotators. This study investigates these dependencies in the case of arthroscopic release of IFS.

Methods: The study group comprised 23 patients (average aged 54.2) who underwent arthroscopic release due to IFS and 20 healthy volunteers. The average follow-up time was 29.2 months. The Biodex system was used for proprioception measurement in a modified neutral arm position and isokinetic evaluation. The results were analysed using the T-test, Wilcoxon and interclass correlation coefficient. *P*-values lower than 0.05 were considered significant.

Results: Statistically significant differences were found between involved (I) and uninvolved (U) shoulders only in the cases of PJPS and AJPS, peak torque, time to peak torque and acceleration time for ER ($p < 0.05$). No statistically significant difference was noted between PJPS IR and PJPS ER or between AJPS IR and AJPS ER ($p > 0.05$) for the U shoulders.

Conclusions: The anatomical structure of anterior (capsule, middle and anterior band of inferior gleno-humeral ligament) and posterior (capsule and posterior band of inferior gleno-humeral ligament) passive shoulder restraints has no impact on the difference in PJPS values between ER and IR in a modified neutral shoulder position. The potential for spontaneous healing of the anterior and posterior passive shoulder restraints influences PJPS recovery after arthroscopic release of IFS. ER peak torque deficits negatively affect AJPS values. PJPS and AJPS of ER and IR can be measured with a high level of reproducibility using an isokinetic dynamometer with the arm in a modified neutral shoulder position. Differences greater than 15 % for PJPS and >24 % for AJPS for ER and IR can be helpful for future studies as baseline data for identification of particular passive and active shoulder stabilizers at risk.

Keywords: Frozen shoulder, Isokinetics, Proprioception, Passive stabilizers

Background

The most frequently studied forms of shoulder joint proprioception are passive and active joint position sense (PJPS and AJPS) [1–10]. However, knowledge regarding proprioception dysfunctions remains incomplete, and the potential for passive shoulder stabilizers to spontaneously heal, as well as the relationship between the healing process and the position senses, is not fully understood [1, 3, 4, 6, 7,]. Hence, the precise relationship between the anatomical structure of the anterior and posterior passive shoulder stabilizers and PJPS or AJPS remains unclear, and relationship between them and the isokinetic muscle performance demands further clarification. Similarly, previous studies have been unable to reach consensus on the optimal position and equipment which should be used for measurement and normative PJPS and AJPS values [1–10].

A recent literature review reveals a lack of research concerning the evaluation of PJPS and AJPS after

arthroscopic capsule-ligamentotomy for idiopathic frozen shoulder (IFS), despite it being one of the most common disorders of the soft tissues of the shoulder joint [11]. Selective release of the anterior-inferior-posterior joint capsule, medial gleno-humeral ligament (MGHL) and inferior gleno-humeral ligament (IGHL) has many advantages: not only is it conscious, precise and reproducible, it is an effective way of treating certain cases and gives positive results [12–17]. Hence, IFS offers great potential for the study of PJPS and AJPS and the relationship between them.

Assuming that the difference between the anatomical structure of the anterior and posterior passive shoulder stabilizers has an impact on proprioception and its spontaneous recovery after arthroscopic release of idiopathic frozen shoulder, the aims of this study were as follows: 1) to evaluate the influence of the anterior and posterior capsule (AC and PC), the middle gleno-humeral ligament (MGHL) and the anterior and posterior bands of inferior gleno-humeral ligament (ABIGHL and PIGHL) on the PJPS and AJPS values for internal and external rotation (IR, ER) after arthroscopic release, with regard to the isokinetic performance of the shoulder rotators; 2) to evaluate the reproducibility and clinical value of measur-ing proprioception under minimal stimulation of pro-prioreceptors thanks to the modified neutral position of the arm (MNP) [18] with the use of an isokinetic dyna-mometer; 3) to create a baseline data of normative PJPS and AJPS values for IR and ER for future studies.

Methods

The study group included 23 patients (16 female and 7 male) aged 54.2 (range 37–67) of 27 [16] who underwent arthroscopic capsule-ligamentotomy due to idiopathic frozen shoulder (IFS). The average follow up time was 29.2 months (range, 26–47.3). The operation was performed at least 6 months after non-surgical treatment, which had demonstrated no improvement. The surgical procedure involved limited antero-posterior synovectomy (ablator Linvatec), interval resection and antero-inferior capsule resection, together with both MGHL and IGHL and posterior capsule resection with punch [16], The procedure was conducted by one surgeon (first author). Rehabilitation, comprising both passive and active exercises, was initiated soon after the patient regained consciousness, beginning the first post-operative day. All the patients were subjected to the same rehabilitation protocol mode: continuous passive motion device exercises (2 × 30 min) scapula and shoulder mobilization, as well as isometric and isotonic exercises of the shoulder abductors, external/internal rotators and the shoulder itself. At home, the patients performed stretching exercises and isometric and isotonic exercises of the aforementioned muscles three times a day for 20–30 min. No abduction splints were used.

The measurement protocol was approved by the Medical University of Lodz Bioethics Committee (RNN/193/12/KB). The patients who met the study inclusion criteria were familiarized with the study protocol and gave their written consent to the study before taking part.

The following study group inclusion criteria were adopted: the patient was at last 2 years from arthroscopic release; the patient had undergone a unilateral capsule-ligamentotomy procedure due to idiopathic frozen shoulder in the stage 2 (sever limitation of motion combine with some relief of pain) ((limitation of all shoulder motions, negative x-ray and sonographic evaluation); a negative history of diabetes and previous injuries for both the operated and healthy shoulder; an absence of shoulder pain (involved and contralateral) and neurological deficits of upper extremities at the time of the measurement; more than 90 % of anterior flexion, internal and external rotation present at 90° abduction in the scapular plane; the patient was able to undergo the intended measurements.

A Biodex System 3 isokinetic dynamometer (Biodex, Inc, USA) was used to measure all proprioception components and muscle performance. Prior to the measurement, the system was calibrated according to the instructions and recommendations of the producer. Before the measurement, each patient was given a thorough explanation of the study methodology and instructed as to the accuracy of the measure and the mode of communication with the researcher. The APJS and PJPS values of the gleno-humeral joint of the patients who met the given study inclusion criteria were measured on both the uninvolved (U) and involved (I) sides during IR and ER. When completing the measurement protocol, the U limb was tested first. The measurement was repeated 3 times and the obtained values were averaged and subjected to statistical analysis. Additionally, intraclass correlation coefficients (ICC) were used to determine the test-retest reliability of proprioception measurement in 20 randomly-selected healthy volunteers (10 male and 10 female; average age 24.5 years, range 18–38). All underwent PJPS and AJPS evaluation with two investigators who had been trained in the same protocol evaluation. Each subject completed a questionnaire regarding medical history to rule out subjects with neuromuscular or musculoskeletal injuries. Subject selection criteria included no history of upper extremity pathology or injury, a range of motion with a similar extent as the U side in the study group, as well as negative neurological and sonographic evaluations of the shoulders. Each subject was required to sign an informed consent form. Two test sessions were scheduled 4 days apart and were carried out at approximately the same time of day to ensure consistent activity levels.

Proprioception measurements were carried out with patients seated. To limit visual and acoustic stimuli

during the procedure, bands were placed over the eyes of the patients and ear plugs were inserted. The patients were also stabilized with shoulder (both right and left) and hip straps fastened to the chair. To limit sensory stimuli from the skin during the proprioception test, the forearm in contact with the dynamometer was placed in an air splint (URIAS splint, Johnstone, 40–50 cm long). During both the AJPS and PJPS tests, the patient held a remote control which could be used to stop the dynamometer in the required position.

The proprioception measurements on the dynamometer were carried out in the MNP: the dynamometer was tilted 30° from horizontal base position, and the glenohumeral joint placed at 30° of abduction and 30° of forward flexion into the plane of the scapula [18] (Fig. 1).

The active and passive joint position senses of glenohumeral joint measurement

For AJPS evaluation at 30° external and internal rotation, the time between trials for external and internal rotation was 60 s. Before each trial, the patient was presented with a position which had to be actively imitated. The time to memorize the position was 10 s. After reaching the re-quired joint position, the patient pressed the button to block the dynamometer. For PJPS evaluation at 30° ER and IR, the protocol was similar but the dynamometer arm initiated the motion in the given direction from the initial position at a constant angular velocity of 1° /s.

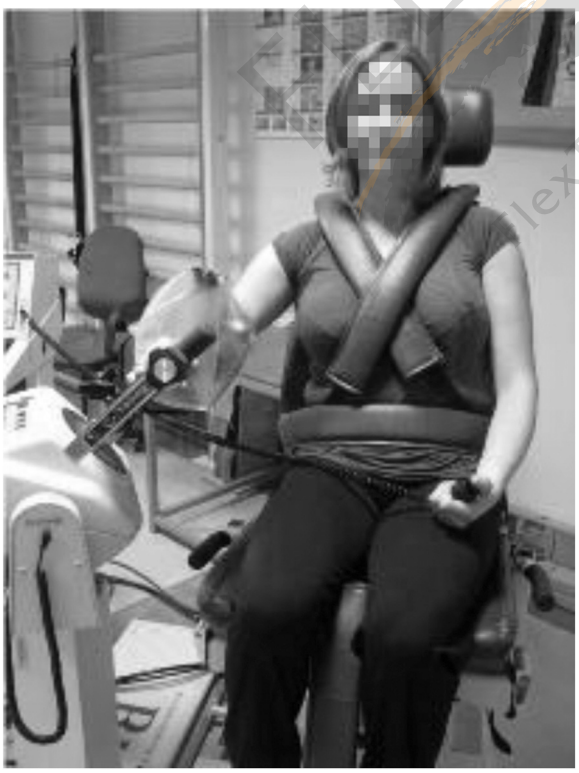

Fig. 1 Modified neutral shoulder position

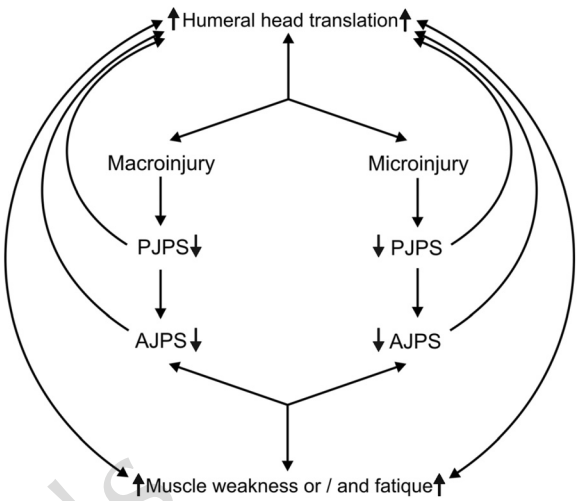

Fig. 2 The concept of the vicious circle of the dependencies between passive and active joint position sense (PJPS and AJPS), macro- and micro-injury of passive stabilizers and muscle performance

Isokinetic evaluation of internal and external rotation

Isokinetic evaluation of ER and IR was performed in the MNP with 180° speed [18]. The peak torque, average peak torque, time to peak torque, acceleration and deceleration times were measured and then used for further statistical evaluation.

Statistical analysis

The arithmetic mean and standard deviation were calculated from basic position measurements. The Shapiro-Wilk test was used to test the distribution of the data. For mean values with normal distributions, the parametric Student's t-test for dependent samples was used to identify statistically significant differences between the operated (I) and unoperated (U) limbs. For non-normal variables, the non-parametric rank-sum Wilcoxon test was implemented. Additionally, the Intraclass Correlation Coefficient (ICC) was used to evaluate the test-retest reliability of the measurements. A significance level of $p < 0.05$ was accepted. All the calculations were performed with STATISTICA ver.10 (StatSoft, Inc. 2011).

Results

Statistically significant differences were found between the I and U shoulders only in the cases of PJPS and AJPS for ER (Table 1). The isokinetic evaluation revealed statistically significant differences between controls and the operated shoulders regarding peak torque, average peak torque, time to peak torque and acceleration time for ER and time to peak torque for IR (Table 1). No statistically

Table 1 Basic data of active and passive joint position senses (AJPS, PJPS) for internal and external rotation (IR and ER) and isokinetic parameters for 180° speed for the involved (I) and uninvolved (U) shoulders of 23 patients operated on for idiopathic frozen shoulder, with statistical data regarding the particular comparisons between them (Wilcoxon test; $p < 0.05$)

Parameters	Shoulder	Mean	SD	Range	*p* Value
AJPS IR ^{0}	I	5.03	3.53	1.3–15.3	0.054
	U	3.84	1.97	2.0–10.3	
AJPS ER^{0}	I	6.56	3.52	2.0–14.3	0.013
	U	4.71	2.50	1.7–11	
PJPS IR^{0}	I	4.23	1.41	2.3–7.3	0.112
	U	3.59	1.44	1.7–6.0	
PJPS ER^{0}	I	5.37	2.48	2.0–12.3	0.024
	U	3.80	1.82	1.3–7.3	
Peak Torque IR (Nm)	I	16.60	11.98	3.0–52.9	0.187
	U	18.30	11.37	3.2–46.6	
Peak Torque ER (Nm)	I	13.76	8.67	2.2–34.6	0.011
	U	15.82	7.09	6.8–32.8	
Average Peak Torque IR (Nm)	I	14.60	11.76	2.5–51.3	0.119
	U	16.35	10.66	2.2–41.3	
Average Peak Torque ER (Nm)	I	12.44	8.31	1.2–32.0	0.015
	U	14.27	7.04	4.8–32.2	
Time to Peak Torque IR (msec)	I	432.17	151.81	230–800	0.003
	U	364.78	117.20	210–650	
Time to Peak Torque ER (msec)	I	423.91	237.04	180–1120	0.012
	U	332.61	110.83	200–680	
Acceleration time IR (msec)	I	256.52	96.18	100–490	0.196
	U	250.44	109.77	100–530	
Acceleration time ER (msec)	I	286.52	118.19	100–560	0.007
	U	230	74.53	110–380	
Deceleration time IR (msec)	I	335.23	133.07	130–650	0.224
	U	301.74	138.36	130–600	
Deceleration time ER (msec)	I	280	120.30	130–590	0.284
	U	251.3	107.51	100–480	

significant differences were noted between PJPS IR and PJPS ER ($p = 0.738$) or between AJPS IR and AJPS ER ($p = 0.132$) for the U shoulder (Table 1).

The interclass correlation coefficients (ICC) of 40 shoulders of 20 healthy volunteers confirm that using a Biodex dynamometer to measure PJPS and AJPS with the arm in the MNP allows proprioception to be assessed with high reliability (Table 2).

The relationship between two consecutive measurements of AJPS and PJPS, for both IR and ER, for the healthy volunteers was not significant. Similarly, the comparison between the average values of IR PJPS and ER PJPS was insignificant, as was the relationship between the average values of IR AJPS and ER AJPS (Table 3).

Discussion

This is the first study to confirm that the anatomical structure of the anterior (capsule, MGHL, ABIGHL) and posterior (capsule and PBIGHL) passive shoulder restraints has no impact on the range of PJPS for either ER or IR, and that their potential for spontaneous healing affects the recovery of proprioception after arthroscopic release of idiopathic frozen shoulder. Previous studies of shoulder proprioception have used various sets of equipment and a range of arm positions [1–10, 19–24]. One of the devices used to study proprioception is the isokinetic dynamometer [1, 6, 10, 20], which allows measurement of the peak torque of the muscle responsible for shoulder stability and injury prevention [18, 24,].

Table 2 The average values, standard deviation (SD) and range of active and passive joint position sense (AJPS and PJPS) for internal and external rotation (IR and ER) of 40 shoulders from 20 healthy volunteers, together with the test retest evaluation of the inter-observer correlation coefficient (ICC) between 2 measurements

	Measurement (°)		ICC
	1	2	
AJPS IR	2.94 (1.25), 1.0–5.8	3.00 (1.11), 1.0–5.2	0.97
AJPS ER	2.87 (1.33), 0.9–6.1	2.89 (1.09), 1.2–5.2	0.95
PJPS IR	2.40 (1.34), 0.3–5.3	2.64 (1.16), 1.0–5.0	0.96
PJPS ER	2.39 (1.38), 0.3–5.3	2.55 (1.26), 0.4–5.1	0.96

Shoulder position plays a crucial role in interpreting the results of PJPS and AJPS assessment. Since more tension is created in the passive and active restraints, and thus the tension of their respective mechanoreceptors, Golgi organs and muscle spindles, at the terminal points of the range of motion [25–28], this influences the assessment of PJPS and AJPS. Massimini et al. [27] note that the elongation of the MGHL, the anterior band of the IGHL (ABIGHL) and the posterior band of the IGHL (PBIGHL) are less at 45° of abduction than at 90° of abduction and at 90° of abduction combined with ER and IR. Thus, placing the arm in the MNP allows relatively minimal tension to be placed on particular passive shoulder restraints. This, together with the fact that the isokinetic dynamometer provides stable and precise arm support, combined with reduction of rotator cuff and scapular muscle tension [18] the MNP offers very good sensitivity for measuring PJPS and AJPS for ER and IR. Moreover, the MNP is also very close to 45° of abduction in the scapular plane, which has been demonstrated to facilitate reliable isokinetic assessment of shoulder IR and ER strength [29, 30].

One unexpected finding of our study was the lack of statistically significant differences between the PJPS values measured for ER and IR, both for U shoulders and within the group of healthy volunteers. This indicates that anatomical differences between anterior and posterior passive stabilizers, and differences in the distribution of the particular types of mechanoreceptors contained therein [31–35], do not affect PJPS in MNP.

Table 3 The comparison between two consecutive measurements of active and passive joint position sense (AJPS and PJPS) for internal and external rotation (IR and ER) of 40 shoulders within the group of 20 healthy volunteers (Wilcoxon test: p was significant at < 0.05)

Parameters	p Value
AJPS 1st measurement IR/ER	0.73
AJPS 2nd measurement IR/ER	0.45
PJPS 1st measurement IR/ER	0.95
PJPS 2nd measurement IR/ER	0.51
Average AJPS IR/ER	0.6
Average PJPS IR/ER	0.58

Our study is the first to reveal the spontaneous ability of the PC and PBIGHL to heal and recover sufficient tension for normalization of IR PJPS post-capsuloligamentotomy in idiopathic frozen shoulder. However, in the case of ER rotation, the more complex anatomical structure and wider area of insertion of the MGHL and ABIGHL, in contrast to PBIGHL [33], did not allow sufficient spontaneous healing to take place and for PJPS to be normalized. These findings also support earlier data indicating that the capsule mechanoreceptors influences shoulder proprioception [31, 34, 35].

The results of isokinetic testing are even more convincing (Table 1). The isokinetic test and results of AJPS and PJPS evaluation strongly suggest that besides the impairment of muscle peak torque and time to peak torque, AJPS was also dependent on afferent information from mechanoreceptors of the passive stabilizers while in the MNP (Table 1). In particular, no statistically significant difference was found between I and U with regard to deceleration time for ER (Table 1). Hence, a thorough evaluation of the passive stabilizers should be performed in the case of AJPS impairment [36].

These observations have particular clinical significance. In the case of passive stabilizer insufficiency, the "stability over mobility" mechanism is activated [37]. Although this mechanism allows greater control over shoulder stability, it can impair the function of the shoulder further by influencing the neuromuscular control of agonists and antagonists [37–42]. Wuelker et al. [43] report a 46 % increase of anterior humeral head displacement and 31 % increase of posterior humeral head displacement when rotator cuff forces are reduced by 50 %, and von Eisenhart-Rothe et al. [44] confirm the importance of arm position and muscle activity for gleno-humeral translation in patients with traumatic shoulder instability. Therefore, even subtle injury of the passive stabilizers may influence the PJPS and ultimately, shoulder stability, especially in case of decreased muscle peak torque [40–45]. Furthermore, as muscle fatigue decreases the peak torque and the AJPS value of the shoulder [24, 45], the tensile stress placed on the passive restraints during overhead activities further increases. Therefore, our findings support those of earlier studies, which indicate that, together with careful clinical and proprioception examination, isokinetic testing should be a part of any global shoulder function evaluation in overhead sport activities [18, 24, 38, 46]. Figure 2 summarizes the author's concept of the vicious circle of the dependencies between PJPS and AJPS, passive stabilizers, macro- and micro-injury of passive stabilizers and muscle performance.

The present study has some limitations. The age of the patients is one factor, as proprioception is known to deteriorate with age [47]. However, as the deterioration of proprioception is the result of similar structural and functional changes within both anterior and posterior shoulder passive stabilizers, nervous system and the muscles employed for IR and ER, its decline should not result in significant differences in PJPS and AJPS between the control and operated shoulders examined in the present study. Changes in the passive restraints caused by the inflammatory nature of idiopathic frozen shoulder may also influence the results. As the presence of synovitis prevented any determination of the degree of formation of the MGHL in some cases, no such assessment was included in the study. As the MGHL is somewhat visible in 42 %, distinct in 49 % and clearly visible in 9 % of cases, based on the classification of Gohlke et al. [48], the structure was always released, regardless of its variant of formation.

As the measurement of proprioception in the proposed MNP using an isokinetic dynamometer was found to have very good reliability, it may serve as a standard means of identifying PJPS and AJPS disorders in shoulder IR and ER in overhead sports activities. Furthermore, measurements performed before and after the injury, as well as before, during and at the end of the season [49, 50], may allow for early detection of proprioception disorders, and prevent the damage extending to the passive stabilizers of the shoulder by the implementation of an appropriate rehabilitation procedure [18, 38, 51, 52]. Moreover, the results also suggest that ignoring the time required for passive shoulder stabilizer damage to heal, disregarding its neuroplasticity potential [52], and returning to sporting activities too early do not in fact shorten breaks in career, but extend them. Such activities lead to long-term damage [50, 51] requiring surgical repair, which significantly prolongs these breaks and, in at least 20 % of cases, makes it almost impossible to return to previous levels of overhead sport activity [53].

Our results indicate that differences greater than 15 % for PJPS and greater than 24 % (Table 1) for AJPS for ER and IR can an effective way of identifying shoulders at risk in overhead sport activities. Since differences between 10 to 15 % are acceptable in the case of isokinetic testing [18], and it seems justified to express the limits as percentages rather than degrees as doing so provides a more accurate picture of proprioception. Although the extrapolation of our results to the overhead sport activity population has certain limitations, our findings nevertheless constitute a set of baseline normative PJPS and AJPS values for IR and ER of the shoulder which may be valuable in future studies on arms in the MNP position using an isokinetic dynamometer.

Conclusions

1. The anatomical structure of the anterior and posterior passive shoulder restraints has no impact on differences in PJPS between ER and IR in a modified neutral shoulder position.
2. The potential for spontaneous healing of anatomical structure of the anterior and posterior passive shoulder restraints influences the recovery of PJPS after arthroscopic release of idiopathic frozen shoulder.
3. Deficits of external rotator peak torque negatively affect AJPS.
4. The use of an isokinetic dynamometer with the arm in the modified neutral shoulder position allows the PJPS and AJPS of ER and IR to be measured with a high level of reproducibility.
5. Differences greater than 15 % for PJPS and 24 % for AJPS of ER and IR of the shoulder can be helpful in future studies as baseline data for selection of particular active and passive shoulder stabilizers at risk.

Abbreviations

IFS: idiopathic frozen shoulder; PJPS: passive joint position sense; AJPS: active joint position sense; ER: external rotation; IR: internal rotation; I: involved; U: uninvolved; ICC: inter-observer correlation coefficient test; MGHL: middle gleno-humeral ligament; IGHL: inferior gleno-humeral ligament; ABIGHL: anterior band of inferior gleno-humeral ligament; PBIGHL: posterior band of inferior gleno-humeral ligament.

Competing interests

The authors declare that they have no competing interests.

References

1. Cuomo F, Birdzell MG, Zuckerman JD. The effect of degenerative arthritis and prosthetic arthroplasty on shoulder proprioception. J Shoulder Elbow Surg. 2005;14:345–8. doi:10.1016/j.jse.2004.07.009.
2. Hung Y, Darling WG. Shoulder position sense during passive matching and active positioning tasks in individuals with anterior shoulder instability. Phys Ther. 2012;92:563–73. doi:10.2522/ptj.20110236.
3. Lephart SM, Warner JJ, Borsa PA, Fu FH. Proprioception of the shoulder joint in healthy, unstable, and surgically repaired shoulders. J Shoulder Elbow Surg. 1994;3:371–80. doi:10.1016/S1058-2746(09)80022-0.
4. Lephart SM, Myers JB, Bradley JP, Fu FH. Shoulder proprioception and function following thermal capsulorraphy. Arthroscopy. 2002;18:770–8.

5. Maenhout AG, Palmans T, De Muynck M, De Wilde LF, Cools AM. The impact of rotator cuff tendinopathy on proprioception, measuring force sensation. J Shoulder Elbow Surg. 2012;21:1080–6. doi:10.1016/j.jse.2011.07.006.
6. Rokito AS, Birdzell MG, Cuomo F, Di Paola MJ, Zuckerman JD. Recovery of shoulder strength and proprioception after open surgery for recurrent anterior instability: a comparison of two surgical techniques. J Shoulder Elbow Surg. 2010;19:564–9. doi:10.1016/j.jse.2009.09.010.
7. Warner JP, Lephart S, Fu FH. Role of proprioception in pathoetiology of shoulder instability. Clin Orthop Relat Res 1996;330:35–9.
8. Yang J-L, Chen S, Jan M-H, Lin YF, Lin JJ. Proprioception assessment in subjects with idiopathic loss of shoulder range of motion: joint position sense and a novel proprioceptive feedback index. J Orthop Res. 2008;26:1218–24. doi:10.1002/jor.20627.
9. Fyhr C, Gustavsson L, Wassinger C, Sole G. The effects of shoulder injury on kinaesthesia: A systematic review and meta-analysis. Man Ther. 2015;20:28–37. doi:10.1016/j.math.2014.08.006.
10. Alvemalm A, Furness A, Wellington L. Measurement of shoulder joint kinaesthesia. Manual Therapy. 1996;1:140–5. doi:10.1054/math.1996.0262.
11. Juel NG, Natvig B. Shoulder diagnoses in secondary care, a one year cohort. BMC Musculoskelet Disord. 2014;15:89. doi:10.1186/1471-2474-15-89.
12. Baums MH, Spahn G, Nozaki M, Steckel H, Schultz W, Klinger HM. Functional outcome and general health status in patients after arthroscopic release in adhesive capsulitis. Knee Surg Sports Traumatol Arthrosc. 2007;15:638–44. doi:10.1007/s00167-006-0203-x.
13. Jerosch J. 360° arthroscopic capsular release in patients with adhesive capsulitis of the glenohumeral joint–indication, surgical technique, results. Knee Surg Sports Traumatol Arthrosc. 2001;9:178–86.
14. Lafosse L, Boyle S, Kordasiewicz B, Aranberri-Gutiérrez M, Fritsch B, Meller R. Arthroscopic arthrolysis for recalcitrant frozen shoulder: a lateral approach. Arthroscopy. 2012;28:916–23. doi:10.1016/j.arthro.2011.12.014.
15. Warner JJ, Allen A, Marks PH, Wong P. Arthroscopic release for chronic, refractory adhesive capsulitis of the shoulder. J Bone Joint Surg Am. 1996;78:1808–16.
16. Waszczykowski M, Polguj M, Fabiś J. The impact of arthroscopic capsular release in patients with primary frozen shoulder on shoulder muscular strength. Biomed Res Int. 2014;2014:834283. doi:10.1155/2014/834283.
17. Berghs BM, Sole-Molins X, Bunker TD. Arthroscopic release of adhesive capsulitis. J Shoulder Elbow Surg. 2004;13:180–5. doi:10.1016/S1058274603003094.
18. Ellenbecker TS, Davies GJ. The Application of Isokinetics in Testing and Rehabilitation of the Shoulder Complex. J Athl Train. 2000;35:338–50.
19. Allegrucci M, Whitney SL, Lephart SM, Irrgang JJ, Fu FH. Shoulder kinesthesia in healthy unilateral athletes participating in upper extremity sports. J Orthop Sports Phys Ther. 1995;21:220–6. doi:10.2519/jospt.1995.21.4.220.
20. Laudner KG, Meister K, Kajiyama S, Noel B. The relationship between anterior glenohumeral laxity and proprioception in collegiate baseball players. Clin J Sport Med. 2012;22:478–82. doi:10.1097/JSM.0b013e31826903f5.
21. Lubiatowski P, Ogrodowicz P, Wojtaszek M, Kaniewski R, Stefaniak J, Dudziński W, et al. Measurement of active shoulder proprioception: dedicated system and device. Eur J Orthop Surg Traumatol. 2013;23:177–83. doi:10.1007/s00590-012-0950-y.
22. Riemann BL, Myers JB, Lephart SM. Sensorimotor System Measurement Techniques. J Athl Train. 2002;37:85–98.
23. Swanik KA, Lephart SM, Swanik CB, Lephart SP, Stone DA, Fu FH. The effects of shoulder plyometric training on proprioception and selected muscle performance characteristics. J Shoulder Elbow Surg. 2002;11:579–86. doi:10.1067/mse.2002.127303.
24. Iida N, Kaneko F, Aoki N, Shibata E. The effect of fatigued internal rotator and external rotator muscles of the shoulder on the shoulder position sense. J Electromyogr Kinesiol. 2014;24:72–7. doi:10.1016/j.jelekin.2013.10.008.
25. Burkart AC, Debski RE. Anatomy and function of the glenohumeral ligaments in anterior shoulder instability. Clin Orthop Relat Res 2002;400:32–9.
26. Janwantanakul P, Magarey ME, Jones MA, Dansie BR. Variation in shoulder position sense at mid and extreme range of motion. Arch Phys Med Rehabil. 2001;82:840–4. doi:10.1053/apmr.2001.21865.
27. Massimini DF, Boyer PJ, Papannagari R, Gill TJ, Warner JP, Li G. In-vivo glenohumeral translation and ligament elongation during abduction and abduction with internal and external rotation. J Orthop Surg Res. 2012;7:29. doi:10.1186/1749-799X-7-29.
28. Suprak DN, Osternig LR, van Donkelaar P, Karduna AR. Shoulder joint position sense improves with elevation angle in a novel, unconstrained task. J Orthop Res. 2006;24:559–68. doi:10.1002/jor.20095.
29. Edouard P, Samozino P, Julia M, Gleizes Cervera S, Vanbiervliet W, Calmels P, et al. Reliability of isokinetic assessment of shoulder-rotator strength: a systematic review of the effect of position. J Sport Rehabil. 2011;20:367–83.
30. Malerba JL, Adam ML, Harris BA, Krebs DE. Reliability of dynamic and isometric testing of shoulder external and internal rotators. J Orthop Sports Phys Ther. 1993;18:543–52. doi:10.2519/jospt.1993.18.4.543.
31. Gohlke F, Janssen E, Leidel J, Heppelmann B, Eulert J. Histopathological findings in the proprioception of the shoulder joint. Orthopade. 1998;27:510–7.
32. Guanche CA, Noble J, Solomonow M, Wink CS. Periarticular neural elements in the shoulder joint. Orthopedics. 1999;22:615–7.
33. O'Brien SJ, Neves MC, Arnoczky SP, Rozbruck SR, Dicarlo EF, Warren RF. The anatomy and histology of the inferior glenohumeral ligament complex of the shoulder. Am J Sports Med. 1990;18:449–56.
34. Vangsness Jr CT, Ennis M, Taylor JG, Atkinson R. Neural anatomy of the glenohumeral ligaments, labrum, and subacromial bursa. Arthroscopy. 1995;11:180–4.
35. Jerosch J, Castro WH, Halm H, Drescher H. Does the glenohumeral joint capsule have proprioceptive capability? Knee Surg Sports Traumatol Arthrosc. 1993;1:80–4.
36. Guanche C, Knatt T, Solomonow M, Wink CS. The synergistic action of the capsule and the shoulder muscles. Am J Sports Med. 1995;23:301–6.
37. Borsa PA, Laudner KG, Sauers EL. Mobility and stability adaptations in the shoulder of the overhead athlete: a theoretical and evidence-based perspective. Sports Med. 2008;38:17–36.
38. Wilk KE, Meister K, Andrews JR. Current concepts in the rehabilitation of the overhead throwing athlete. Am J Sports Med. 2002;30:136–51.
39. Diederichsen L, Krogsgaard M, Voigt M, Dyhre-Poulsen P. Shoulder reflexes. J Electromyogr Kinesiol. 2002;12:183–91.
40. Escamilla RF, Yamashiro K, Paulos L, Andrews JR. Shoulder muscle activity and function in common shoulder rehabilitation exercises. Sports Med. 2009;39:663–85. doi:10.2165/00007256-200939080-00004.
41. Glousman R, Jobe F, Tibone J, Moynes D, Antonelli D, Perry J. *Dy*namic electromyographic analysis of the throwing shoulder with glenohumeral instability. J Bone Joint Surg Am. 1988;70:220–6.
42. Myers JB, Ju Y-Y, Hwang J-H, McMahon PJ, Rodosky MW, Lephart SM. Reflexive muscle activation alterations in shoulders with anterior glenohumeral instability. Am J Sports Med. 2004;32:1013–21.
43. Wuelker N, Korell M, Thren K. Dynamic glenohumeral joint stability. J Shoulder Elbow Surg. 1998;7:43–52.
44. Von Eisenhart-Rothe RMO, Jäger A, Englmeier K-H, Vogl TJ, Het G. Relevance of arm position and muscle activity on three-dimensional glenohumeral translation in patients with traumatic and atraumatic shoulder instability. Am J Sports Med. 2002;30:514–22.
45. Lee H-M, Liau J-J, Cheng C-K, Tan CM, Shih JT. Evaluation of shoulder proprioception following muscle fatigue. Clin Biomech (Bristol, Avon). 2003;18:843–7.
46. Yildiz Y, Aydin T, Sekir U, Kiralp MZ, Hazneci B, Kalyon TA. Shoulder terminal range eccentric antagonist/concentric agonist strength ratios in overhead athletes. Scand J Med Sci Sports. 2006;16:174–80. doi:10.1111/j.1600-0838.2005.00471.x.
47. Herter TM, Scott SH, Dukelow SP. Systematic changes in position sense accompany normal aging across adulthood. J Neuroeng Rehabil. 2014;11:43. doi:10.1186/1743-0003-11-43.
48. Gohlke F, Essigkrug B, Schmitz F. The pattern of the collagen fiber bundles of the capsule of the glenohumeral joint. J Shoulder Elbow Surg. 1994;3:111–28. doi:10.1016/S1058-2746(09)80090-6.
49. Buss DD, Lynch GP, Meyer CP, Huber SM, Freehill MQ. Nonoperative Management for In-Season Athletes With Anterior Shoulder Instability. Am J Sports Med. 2004;32:1430–3. doi:10.1177/0363546503262069.
50. Dickens JF, Owens BD, Cameron KL, Kilcoyne K, Allred CD, Svoboda SJ, et al. Return to play and recurrent instability after in-season anterior shoulder instability: a prospective multicenter study. Am J Sports Med. 2014;42:2842–50. doi:10.1177/0363546514553181.
51. Niederbracht Y, Shim AL, Sloniger MA, Paternostro-Bayles M, Short TH. Effects of a shoulder injury prevention strength training program on

Clinical outcome of arthroscopic capsular release for frozen shoulder: essential technical points in 255 patients

Abstract

Background: The purpose of this study was to investigate the long-term clinical outcome and its related factors regarding the severity of adhesion of CH ligament over long head of biceps (LHB) after shoulder arthroscopic capsular release for frozen shoulder with technical points in 255 patients.

Methods: We performed arthroscopic capsular release for frozen shoulder in 267 shoulders of 255 patients, 112 males and 143 females, with mean age of 56.39 years, mean disease duration periods of 0.934 years for conservative treatment, and mean follow-up periods of 5.6 years. The frozen shoulders were divided based on the severity of adhesion between CH ligament over LHB: those with slight degree of synovitis, no adhesion by obtuse rod, and slight thickness of the released capsule (type A), those with moderate degree of synovitis, moderate adhesion of the LHB by obtuse rod, and moderate thickness of the released capsule (type B), and those with severe degree of synovitis, severe adhesion of the LHB by obtuse rod, and severe thickness of the released capsule adhesion and a flatly shaped LHB (type C). We assessed the clinical factors related to the scoring of the shoulders by the criteria of the American Shoulder and Elbow Surgeons (ASES) and the relationship with severity of LHB adhesion.

Results: The ASES scores improved at 5 years postoperatively in all three groups significantly. The range of motion also significantly improved in all three groups significantly. The severity of the LHB adhesion over the CH ligament was confirmed to influence the ASES scores before and after the arthroscopic capsular release. There was a significant difference between type A and type B ($p < 0.0001$) or type C ($p < 0.0001$) before and after surgery. Logistic regression analysis showed disease duration, diabetes mellitus (DM), and ASES score were significantly associated to the severity type of LHB, especially DM has high odds ratio and was a risk factor for LHB adhesion. There is no adverse event including dislocation or axillary nerve injury and recurrence after arthroscopic capsular release at 5 years after surgery.

Conclusions: The long-term results of arthroscopic capsular release in frozen shoulder were confirmed in 255 patients. The severity of LHB adhesion over the CH ligament, a pathological condition related to DM as a risk factor, seems to play an important role in the functional outcome. Therefore, the sufficient release of LHB was essential technical point for arthroscopic capsular release in frozen shoulder.

Keywords: Frozen shoulder, Arthroscopic capsular release, LHB, CH ligament

Background

While physiotherapy, analgesics for pain, steroid injection, and silent manipulation can all be effective for frozen shoulder, there has been no description of a long term with more than 200 patients of arthroscopic capsular re-lease for frozen shoulder so far. It is reported recently that arthroscopic capsular release for frozen shoulder is effect-ive and safe in several literatures [1–3]. Walther et al. reported that arthroscopic capsular release should be rec-ommended as the early choice for treatment in persistent frozen shoulder in 54 patients [1]. On the other hand, Neviaser used the term "adhesive capsulitis" to reflect his findings in surgery [4]. In pathological aspect, the thick-ness of the coracohumeral (CH) ligament over 4 mm and joint capsule over 7 mm by MRI was important to the diagnosis of frozen shoulder [5]. In anatomical analysis, the CH ligament was divided into two parts: one part spread fibers over the rotator interval to the posterior portion of the greater tuberosity and the other part enveloped the superior portion of the subscapularis, supraspinatus, and infraspinatus tendons. The anterior CH ligament holds the subscapularis muscle and anchors the muscle to the coracoid process in a similar manner to that of the posterior coracohumeral ligament (CHL) enveloping the supraspinatus and infraspinatus over the long head of biceps (LHB) tendon [6]. We previously reported the classification of arthroscopic findings for frozen shoulder based on the LHB adhesion over CH ligament in 87 patients [7]. The hypothesis in this study is that LHB adhesion to CH ligament is associated with the long-term outcome of arthroscopic capsular release in frozen shoulder. The purpose of this study was to investigate the long-term clinical outcome in 255 patients and extract clinical factors related to the efficacy of shoulder arthroscopic capsular release for frozen shoulder.

Methods

Study design

Two hundred and sixty seven consecutive frozen shoulders of 255 patients underwent arthroscopic capsular release admitted in Tokyo Women's Medical University, Medical Center East by a single surgeon (K.K.) from August 2003 including 112 males and 143 females, with mean age of 56.39 ± 10.24, mean disease duration periods 0.934 ± 0.393 years, and mean follow-up periods 5.648 ± 4.060 (range 5–13) years (Table 1). Preoperative treatments for the frozen shoulder included rehabilitation or steroid or hyaluronic acid injections or non-steroid anti-inflammatory drugs (NSAIDs) before arthroscopic capsular release at least more than 6 months. The criteria for inclusion in this study were severe night pain concomitant with no improvement of flexion (90°) and external rotation (0°) and poor responsiveness to rehabilitation for at least 5 to 6 months prior to the surgery recognized on the thickness of CH ligament by MRI [5]. Exclusion criteria were complete rotator cuff tear, acromioclavicular subluxation, and biceps tendon rupture in clinical and MRI findings. The frozen shoulders were divided into three types based on the severity of the adhesion of the LHB to the CH ligament as assessed by arthroscopy (Fig. 1): those with slight degree of synovitis, no adhesion by obtuse rod, and slight thickness of the released capsule (type A), those with moderate degree of synovitis, moderate adhesion of the LHB by obtuse rod, and moderate thickness of the released capsule (type B), and those with severe degree of synovitis, severe adhesion of the LHB by obtuse rod, and severe thickness of the released capsule adhesion and a flatly shaped LHB (type C). The frozen shoulders ($n = 267$) were divided into 162 shoulders of type A shoulders (56.20 ± 11.20 years; range, 23–82 years), 87 shoulders of type B shoulders (56.61 ± 8.06 years; range, 36–76 years), and 18 shoulders of type C shoulders (57.06 ± 11.13 years; range, 35–78 years). Disease duration with conservative treatment before surgery was 0.790 ± 0.271 years in type A, 1.075 ± 0.362 years in type B, 1.556 ± 0.591 years in type C.

Table 1 Baseline characteristics for arthroscopic capsular release

Patient/shoulder number	255/267
Age (years)	56.39 ± 10.24
Female (*n*/%)	143 (53.56)
Disease duration (years)	0.934 ± 0.393
Follow-up period (years)	5.648 ± 4.060
Type A (*n*/%)	162 (60.67)
Type B (*n*/%)	87 (32.58)
Type C (*n*/%)	18 (6.74)
ASES scores at baseline	41.104 ± 5.965
DM (*n*/%)	53 (19.85)

ASES American Shoulder and Elbow Surgeons, *DM* diabetes mellitus

Procedure of arthroscopic capsular release and essential technical points for frozen shoulder: partial capsular release and ASD

After placing the patient in the beach-chair position under general anesthesia or interscalene local anesthetic blockade, the shoulder was examined before surgery to assess the range of motion in flexion and extension, external rotation at 0° abduction, external rotation at 90° abduction, and internal rotation at 90° abduction. After introducing a 4-mm arthroscopy through a standard posterior portal and performing an initial diagnostic arthroscopy, we created an anterior portal just lateral side of coracoid process to superior of the subscapularis tendon using the outside-in technique in order to facilitate maneuvers by instruments such as shavers and a radiofrequency instrument (VAPR®; Mitek, Norwood,

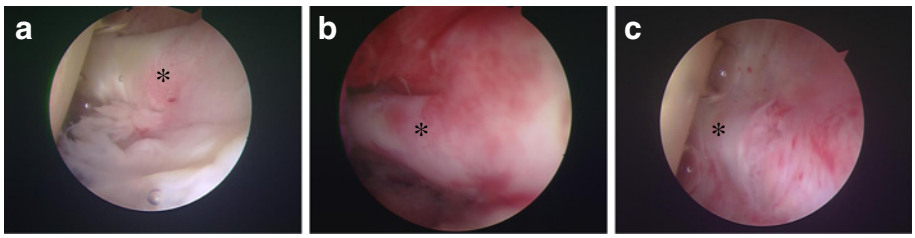

Fig. 1 Arthroscopic classification based on the severity of adhesion of LHB and CH ligament. **a** Slight adhesion to easily get into the back of LHB by obtuse rod. **b** Moderate adhesion to hardly get into the back of LHB by obtuse rod. **c** Severe adhesion with no space to get into the back of LHB by obtuse rod. Asterisk is LHB

MA). Next, we assessed the LHB adhered to the CH ligament over shoulder joint (Fig. 2a). Our first step in the capsular release was to eliminate the adhesion of the LHB to the CH ligament using a radiofrequency instrument. Next, we removed the joint capsule just next to the labrum using a radiofrequency instrument and rasp from 5 o'clock to 11 o'clock of the right-side shoulder over LHB (Fig. 2b). Our method is partial capsular release for frozen shoulder. Thus, we released the anterior, anteroinferior, superior, and superior-posterior capsules in addition to eliminate the LHB adhesion to the CH ligament. Inferior-posterior portion of capsule was remained to maintain shoulder stability and refrain from axillary nerve injury. A rasp conventionally used for arthroscopic Bankart repair proved quite useful in moving the capsule into the neck of the glenoid without axillary nerve complication to move the capsule. After arthroscopically observing the joint, we moved a scope into the subacromial space via a lateral and anterolateral portal, shaved the synovium in the subacromial bursa, and carefully observed the rotator cuff. Arthroscopic subacromial decompression (ASD) was performed and smoothed the surface of rotator cuff and subacromial bursa by using VAPR® and the rasp (Fig. 2c). Then, after removing the scope, we performed the manipulation. Once the scope and instruments were removed, shoulders were manipulated in external rotation at 0° of abduction, external rotation at 90° of abduction, internal rotation at 90° of abduction, and flexion in the plane of the scapula in addition to extension. At the end of the capsular release, the measurement of range of motion obtained after the manipulation was performed. After all procedures, we checked the sliding movement of LHB and wash out intra GH joint to eliminate the coagulation and debris for final step (Fig. 2d). If the insufficient ROM was obtained, the adhesion of LHB should be released again.

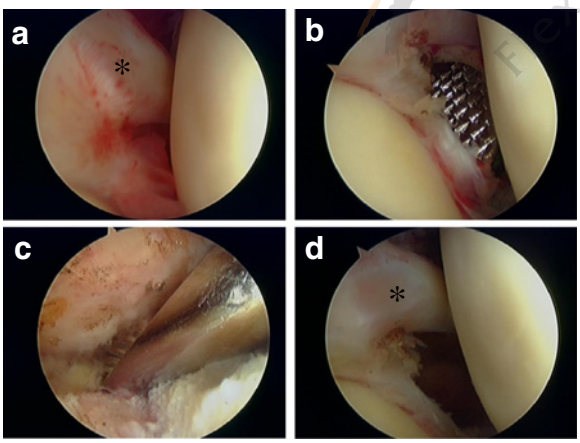

Fig. 2 Procedure of arthroscopic capsular release for frozen shoulder. **a** Arthroscopic finding around LHB with synovium over CH ligament. Asterisk is LHB. **b** Rasp is used just outside of labrum along with the glenoid neck bone. **c** Subacromial decompression was performed concomitantly by using abrader arthroscopically. **d** After arthroscopic capsular release, CH ligament adhered over LHB was removed and joint space was widen clearly

As postoperative rehabilitation protocol, passive, assisted-active exercises and stooping exercise were commenced for forward flexion and external rotation 1 day after surgery with the assistance of a physical therapist. After 2 week of passive exercise, the patients began active exercise to strengthen the rotator cuff and scapular stabilizers. After the rehabilitation for 4 to 6 weeks, the patients were back on normal work schedules without any limitations to daily activity. The rehabilitation was still continued for 3 months after surgery to obtain complete muscle strength of the shoulder.

Measurement of outcome

All patients were assessed by the American Shoulder and Elbow Surgeons (ASES) score preoperatively, and at the final evaluation was performed at an average of 5.648 ± 4.060 years postoperatively [8]. Preoperative and postoperative assessments for the progress of recovery of the range of motion at forward elevation (flexion), external rotation at 0 and 90° of abduction, and internal rotation at 0 and 90° of abduction were performed in the three arthroscopic types (types A, B, and C). Informed consent was obtained from all patients, and the study protocol was approved by the ethics committee of Tokyo Women's Medical University. ASES scores were assessed

in each three groups before and after surgery, and multiple regression analysis with logistic procedure was used for detecting the clinical factors related to the severity of LHB type. The population especially of diabetes mellitus (DM) in each group was analyzed.

Statistical analysis

We used the Wilcoxon test to compare ASES scores [8] and the degrees of range of motion with before and after surgery. Mann-Whitney *U* test was used to compare those results among different types of groups. The logistic regression analysis for LHB type severity was performed including age, disease duration, DM, and ASES scores at baseline and 5 years after surgery. Gender ratio was also calculated in each group. p values < 0.05 were considered to be significant using StatFlex version 6.0 (Statflex, Tokyo, Japan).

Results

The ASES score improved postoperatively in all three groups: from 41.10 ± 5.96 before surgery to 97.81 ± 3.25 at 5 years after surgery in the 267 shoulder joints, including from 43.81 ± 2.15 before surgery to 99.29 ± 1.38 after surgery in the type A shoulder joints (n = 162), from 39.33 ± 4.67 to 96.41 ± 3.24 in type B (n = 87), and from 25.36 ± 7.36 to 91.21 ± 4.17 in type C (n = 18) (Figs. 3 and 4). There was a significant difference between type A and type B ($p < 0.0001$) or type C ($p < 0.0001$) before and after surgery. The range of motion in flexion improved in all three groups postoperatively, from a mean of 80 ± 6.11 to 165 ± 8.84 in type A, from a mean of 75 ± 5.58 to 155 ± 7.96 in type B, and from a mean of 60 ± 6.38 to 140 ± 7.55 in type C. External rotation at 0° of abduction was improved from a mean of – 10 ± 7.32 to 45 ± 6.51 in type A, from a mean of – 15 ± 7.11 to 40 ± 6.89 in type B, and from a mean of – 25 ± 6.98 to 30 ± 7.45 in type C. Internal rotation improved from a mean of S1 to Th12 in type A, from a mean of S2 to L1 in type B, and from a mean of S2 to L1 in type C. Therefore, the range of motion was also confirmed to be dependent on the recovery of LHB adhesion to the CH ligament after surgery. Logistic regression analysis revealed the arthroscopic finding as for type of LHB adhesion related with disease duration ($p = 0.0012$, odds ratio 0.08723, RI 0.02004~0.37964), DM ($p = 0.0005$, odds ratio 6.96680, RI 2.34963~20.6570), ASES score at baseline ($p < 0.0001$, odds ratio 1.56785, RI 1.29615~1.89651), and ASES scores at 5 years ($p = 0.0014$, odds ratio 1.60086, RI 1.19857~2.13819) (Table 2). Furthermore, the percent of DM in each group showed 14.2% in type A, 25.3% in type B, and 44.4% in type C as shown in Fig. 5. DM ratio of type C was significantly higher than that of type A ($p = 0.0012$) and type B ($p = 0.0302$). Female percent was 44.4% in type A, 65.5% in type B, and 77.8% in type C. Female ratio of type C was significantly higher than that of type A ($p = 0.0070$) and type B ($p = 0.0014$). However, logistic analysis showed no significant difference

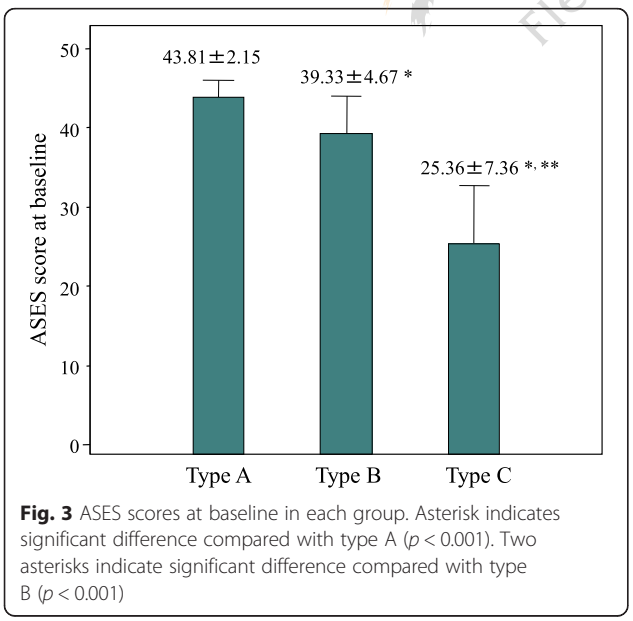

Fig. 3 ASES scores at baseline in each group. Asterisk indicates significant difference compared with type A ($p < 0.001$). Two asterisks indicate significant difference compared with type B ($p < 0.001$)

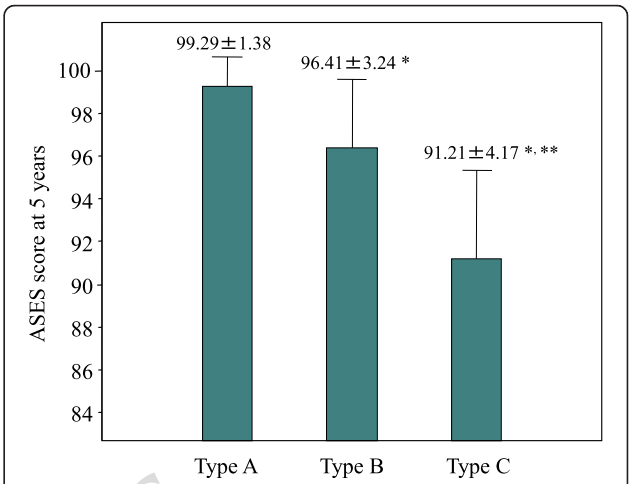

Fig. 4 ASES scores at 5 years after arthroscopic capsular release in each group. Asterisk indicates significantly different compared with type A ($p < 0.001$). Two asterisks indicate significantly different compared with type B ($p < 0.001$)

Table 2 Logistic regression analysis for the type of frozen shoulder

Factors	p value	Odds ratio (RI)
Age	0.8394	1.00381 (0.96759~1.04137)
Disease duration	0.0012	0.08723 (0.02004~0.37964)
DM	0.0005	6.96680 (2.34963~20.6570)
ASES score at baseline	< 0.0001	1.56785 (1.29615~1.89651)
ASES score at 5 years	0.0014	1.60086 (1.19857~2.13819)
Gender	0.0974	1.93661 (0.88640~4.23110)

ASES American Shoulder and Elbow Surgeons, *DM* diabetes mellitus

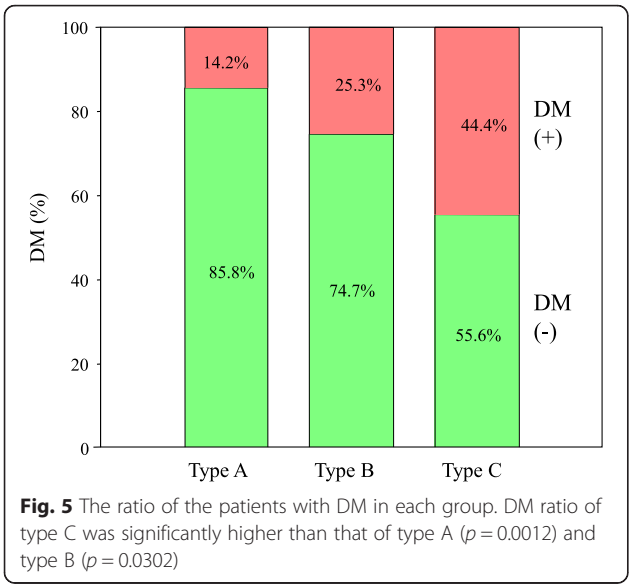

Fig. 5 The ratio of the patients with DM in each group. DM ratio of type C was significantly higher than that of type A ($p = 0.0012$) and type B ($p = 0.0302$)

to the type of LHB ($p = 0.0974$). Therefore, LHB adhesion to the CH ligament related to clinical outcome and DM ratio in frozen shoulder. There was no adverse event including axillary nerve injury or dislocation and recurrence after arthroscopic capsular release in this study.

Discussion

Management of choice involves conservative treatment such as non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular steroids of hyaluronic acid injection, physical therapy, and silent manipulation under cervical nerve root block anesthesia are applied [9–12]. However, Cochrane reviews have demonstrated that the current literature base shows that physiotherapy alone has little to no benefit as compared to control groups [13]. There are a number of adjuncts that are often used with physiotherapy including extracorporeal shockwave therapy, electromagnetic stimulation, acupuncture, and the use of lasers, none of which have been subjected to investigation with randomized controlled studies [14]. Even when undergoing rehabilitative treatment, frozen shoulder often continues to feel severe night pain and contracture enough to disturb shoulder function. In some 10% of cases, indications for arthroscopic capsular release are present and currently, shoulder arthroscopic capsular release is a treatment of choice in such cases [14]. We selected arthroscopic capsular release for recalcitrant adhesive frozen shoulder after unsuccessful rehabilitation. However, the comparison of manipulation and arthroscopic capsular release by systemic review was reported that the quality of evidence available is low and the data available demonstrate little benefit for a capsular release instead of, or in addition to, a manipulation under anesthesia [15]. Ogilvie-Harris et al. attempted to compare manipulation with arthroscopic release on a prospective cohort of 40 patients [16]. The release induced removal of synovium from the rotator interval, release of the anterior glenohumeral ligament and the intra-articular portion of the subscapularis tendon, and finally, division of the anterior half of the inferior capsule. Their results after a follow-up of between 2 and 5 years showed a similar range of movement, but the release had a much better outcome in review literature [17]. However, there was no evidence of the efficacy of arthroscopic capsular release in more than 200 patients in long-term results.

Our first observation in the current investigation was the restriction of dynamic sliding movement of the LHB in frozen shoulder compared with the normal [7]. The LHB stands upward from the IR to ER positions during this movement. The mechanical physiological functions of the shoulder depend quite closely and sensitively on this area of the LHB, especially for ER. After arthroscopic capsular release, the ER improved in the patients who exhibited the dynamic sliding movement of the LHB. Our data indicated that the physiological movement of the LHB to the rotator interval plays a key role in acquiring an improved range of motion in shoulders rated with high ASES scores. Furthermore, MRI findings on frozen shoulder have typically revealed a thickening of the coracohumeral ligament (CHL) [5]. CHL thickness and wide spread was evident in all three types especially in type C.

Frozen shoulder is thought to have an incidence of 3–5% in the general population and up to 20% in those with diabetes [18]. Its peak incidence in between the ages of 40 and 60 is rare outside these age groups and in manual workers [19] and is slightly more common in women. In this study, DM ratio was 19.85% in total cases. Experimental analysis for frozen shoulder, we reported that mechanical stress on the LHB and rotator interval (RI) in the shoulder may induce the tissue around LHB of mitogen-activated protein (MAP) kinases to express nuclear factor (NF)-κB by CD29 in order to develop capsule contracture, producing matrix metalloproteinase (MMP)-3, interleukin(IL)-6, and vascular endothelial growth factor (VEGF) [20]. Therefore, vascularity of capsule in frozen shoulder was evident in arthroscopic finding. DM also expressed those molecule to induce fibrous tissue in the area of the mechanical stress such as CH ligament and LHB. DM was found to be a possible risk factor related to the severity LHB adhesion with CH ligament which was wide spread out abnormally. Therefore, the patient of frozen shoulder with DM should be careful to manage the arthroscopic capsular release especially around LHB.

In technical point of view, the superior release is then extended to reach the long head of biceps and is continued to release the CHL in the plane between the

superior glenoid and supraspinatus. If internal rotation or adduction of the shoulder is significantly restricted then the camera portal can be reversed to anterior portal for a posterior capsular release. Some surgeons complete the inferior release with a gentle manipulation but some surgeons advocate a full 360° capsulectomy under direct vision while accepting the higher risk of iatrogenic injury the axillary nerve [21]. Pearsall et al. performed arthroscopic release of the anteroinferior capsule, the intra-articular portion of the tendon of subscapularis, the superior and middle gleno-humeral ligaments, and the coracohumeral ligament in patients who had been recalcitrant to conservative treatment [22]. Among the 35 patients followed at a mean of 22 months after surgery, 83% had normal or only mildly symptomatic shoulders. These patients also received a tapered 21-day course of oral prednisolone. None of our patients were given oral steroids during the treatment. We consider that 1 month period is the most important window for obtaining better results by rehabilitation after arthroscopic capsular release. Most patients obtain their final range of motion by 4 to 6 weeks after capsular release. We released the anterior, antero-inferior, and superior capsules in addition to eliminating the LHB adhesion to CHL. Detailed arthroscopy assessments of the LHB adhesion revealed the clinical mechanism responsible for the decreased shoulder function associated with frozen shoulder. Limitation of study includes no control study and more long results needed to the recurrence of this procedure, and the mechanism of DM which contributed the severity of adhesion over LHB was still unclear. We found the risk factor of clinical outcome was DM condition. Therefore, it is possible to DM frozen shoulder should be separated to another category compare to idiopathic frozen shoulder in pathologic condition. In the future, arthroscopic capsular release with less pain after surgery should be performed in day surgery for the privilege of the patients with frozen shoulder.

Conclusions

The long-term results of arthroscopic capsular release in frozen shoulder were confirmed in 255 patients. The severity of LHB adhesion over the CH ligament, a pathological condition related to DM as a risk factor, seems to play an important role in the functional outcome. Therefore, the release of LHB was essential technical point for arthroscopic capsular release in frozen shoulder.

Abbreviations

ASES: American Shoulder and Elbow Surgeons; CH: Coracohumeral; DM: Diabetes mellitus; LHB: Long head of biceps

Competing interests

The author declares that he has no competing interests.

References

1. Walther M, Blanke F, Von Wehren L, Majewski M. Frozen shoulder-comparison of different surgical treatment options. Acta Orthop Belg. 2014; 80(2):172–7.
2. Evans JP, Guyver PM, Smith CD. Frozen shoulder after simple arthroscopic shoulder procedures: what is the risk? Bone Joint J. 2015;97(7):963–6.
3. Mubark IM, Ragab AH, Nagi AA, Motawea BA. Evaluation of the results of management of frozen shoulder using the arthroscopic capsular release. Orthop Traumatol Rehabil. 2015;17(1):21–8.
4. Neviaser J. Arthrography of the shoulder joint: study of the findings in adhesive capsulitis of the shoulder. Study of the findings in adhesive capsulitis of the shoulder. J Bone Joint Surg Am. 1962;44(A):1321–59.
5. Mengiardi B, Pfirrmann CW, Gerber C, Hodler J, Zanetti M. Frozen shoulder: MR arthrographic findings. Radiology. 2004;233(2):486–92.
6. Arai R, Nimura A, Yamaguchi K, Yoshimura H, Sugaya H, Saji T, et al. The anatomy of the coracohumeral ligament and its relation to the subscapularis muscle. J Shoulder Elb Surg. 2014;23(10):1575–81.
7. Kanbe K, Inoue K, Inoue Y. The dynamic movement of the long head of the biceps tendon is associated with treatment of frozen shoulder. J Orthop Surg. 2008;16(3):295–9.
8. Michener L, McClure P, Snennett B. American shoulder and elbow surgeons standardized shoulder assessment form, patient self-report section: reliability, validity, and responsiveness. J Shoulder Elb Surg. 2002; 11(6):587–94.
9. Buchbinder R, Hoving JL, Green S, et al. Short course prednisolone for adhesive capsulitis (frozen shoulder or stiff painful shoulder): a randomised, double blind, placebo controlled trial. Ann Rheum Dis. 2004;63(11):1460–9.
10. Le Lievre HM, Murrell GA. Long-term outcomes after arthroscopic capsular release for idiopathic adhesive capsulitis. J Bone Joint Surg Am. 2012;94(13): 1208–16.
11. Grey RG. The natural history of "idiopathic" frozen shoulder. J Bone Joint Surg Am. 1978;60(4):564.

12. Saito T, Sasanuma H, Iijima Y, Kanaya Y, Saito T, Watanabe H, et al. Short-term clinical results of frozen shoulder treated with shoulder manipulation under ultrasound-guided cervical nerve root block at outpatient setting: a case series. J Orthop Sci. 2017;22(2):275–80.
13. Green S, Buchbinder R, Hetrick S. Physiotherapy interventions for shoulder pain. Cochrane Database Syst Rev. 2003;2:CD004258.
14. Buchbinder R, Youd JM, Green S, Stein A, Forbes A, Harris A, et al. Efficacy and cost-effectiveness of physiotherapy following glenohumeral joint distension for adhesive capsulitis: a randomized trial. Arthritis Rheum. 2007; 57(6):1027–37.
15. Grant JA, Schroeder N, Miller BS, Carpenter JE. Comparison of manipulation and arthroscopic capsular release for adhesive capsulitis: a systematic review. J Shoulder Elb Surg. 2013;22(8):1135–45.
16. Ogilvie-Harris D, Biggs D, Fitsialos D, Mackay M. The resistant frozen shoulder. Clin Orthop Relat Res. 1995;319(10):238–48.
17. Robinson CM, Seah KT, Chee YH, Hindle P, Murray IR. Frozen shoulder. J Bone Joint Surg Br. 2012;94(1):1–9.
18. Thomas SJ, McDougall C, Brown ID, Jaberoo MC, Stearns A, Ashraf R, et al. Prevalence of symptoms and signs of shoulder problems in people with diabetes mellitus. J Shoulder Elb Surg. 2007;16(6):748–51.
19. Manske RC, Prohaska D. Diagnosis and management of adhesive capsulitis. Curr Rev Musculoskelet Med. 2008;1(3-4):180–9.
20. Kanbe K, Inoue K, Inoue Y, Chen Q. Inducement of mitogen-activated protein (MAP) kinases in frozen shoulder. J Orthop Sci. 2009;14(1):56–61.
21. Hsu JE, Anakwenze OA, Warrender WJ, Abboud JA. Current review of adhesive capsulitis. J Shoulder Elb Surg. 2011;20(3):502–14.
22. Pearsall AW 4th, Osbahr DC, Speer KP. An arthroscopic technique for treating patients with frozen shoulder. Arthroscopy. 1999;15(1):2–11.

Adhesive capsulitis of the shoulder, treatment with corticosteroid, corticosteroid with distension or treatment-as-usual; a randomised controlled trial in primary care

Abstract

Background: Optimal management for adhesive shoulder capsulitis (frozen shoulder) is currently unclear. We intended to explore whether treatment by intra-articular injections with corticosteroid and distension is more effective than treating with corticosteroids alone or treatment-as-usual in a primary care setting in Norway.

Methods: In this prospective randomised intention to treat parallel study, 106 patients were block randomised to three groups; 36 (analysed 35) receiving steroid injection and Lidocaine (IS), 34 receiving steroid and additional saline as distension (ISD) and 36 had treatment-as-usual (TAU). Intervention groups received four injections within 8 weeks, assessed on 1st visit, at the 4th and 8th week. Outcomes were Shoulder Pain and Disability Index (SPADI), Numerical pain rating scale (NPRS) and passive range of motion (PROM). Postal assessment was repeated after 1 year for SPADI. Patients in the IS and ISD groups were "blinded" for intervention received and the assessor was "blinded" to group allocation.

Results: At baseline there were no differences between groups in outcome measures. There were no statistical significant differences between the intervention groups in SPADI, NPRS and PROM at baseline, at short-term (4-and 8 weeks) or long-term (12 months). There were statistically significant differences ($p < 0.01$) in change scores at short-term for SPADI when comparing the IS and TAU groups (-20.8; CI-28.9 to -12.7), and the ISD and TAU groups (-21.7; CI-29.4 to -14.0), respectively for NPRS (-2.0; CI-2.8 to -1.1 and -2.2; CI-3.0 to -1.4), and for PROM, but not at long-term for SPADI ($p > 0.05$).
Effect size (ES) at 8 weeks was large between both injection groups and TAU (ES 1.2). At 12 months ES was reduced to 0.3 and 0.4 respectively. Transitory side effects as flushing and after-pain were reported by 14 % in intervention groups.

Conclusion: This intention to treat RCT in primary care indicates that four injections with corticosteroid with or without distension, given with increasing intervals during 8 weeks, were better than treatment-as-usual in treatment of adhesive shoulder capsulitis. However, in the long run no difference was found between any of the groups, indicating that natural healing takes place independent of treatment or not.

Trial registration: ClinicalTrials.gov, https://clinicaltrials.gov/ identifier: NCT01570985

Keywords: Adhesive capsulitis, Corticosteroid, Distension, Frozen shoulder

Background

Adhesive capsulitis of the shoulder, also called frozen shoulder, has a prevalence of 2 to 5 % of the general population, but among diabetic patients the prevalence ranged from 11 to 30 % [1, 2]. There is a strong correlation between adhesive capsulitis and other medical conditions such as diabetes, rheumatic disease, heart disease, hyperthyreosis [3]. Adhesive capsulitis occurs mostly in middle age [4–6] and women between 50 and 60 years are most commonly affected [7]. Both shoulders can be affected simultaneously and/or the other side can be affected a few years later [7, 8]. Shoulder stiffness and pain interferes considerably with activities of daily living, and may be associated with increased sick leave in people of working age and incapacity in the elderly.

Adhesive capsulitis is a long-lasting disorder with spontaneous onset of pain and progressive stiffness [9]. It generally involves reduced movement of the gleno-humeral joint in several planes, with most restriction of external rotation, some restriction of abduction and least affection of internal rotation carried out passively, also called the capsular pattern [5, 6]. Adhesive capsulitis is primarily a clinical diagnosis and radiography can be complementary in the diagnosis [10, 11]. Pathophysiologically, thickening and contracture of the inferior capsule [12], contracture of the rotator interval, coraco-humeral ligament and anterior capsule with a combination of synovial inflammation and capsular fibrosis, has been described [10]. Bunker et al. found the histo-pathological picture comparable to Dupuytren's disease of the hand with no inflammation and no synovial involvement [13]. The natural history remains controversial. Earlier studies considered the condition as self-limiting, lasting for 2 to 3 years, reporting that the majority of patients would get almost complete recovery or full recovery [14, 15]. Other authors report long-term pain and stiffness for several years [16–18]. For convenience, the condition is divided into three phases; the painful phase lasting from 3 to 9 months, followed by a freezing phase with progressive stiffness lasting from 4 to 12 months and finally, the recovery phase with gradual return of movement, lasting 5–26 months [19, 20]. Some have divided the condition into four stages, based on the correlation of findings on physical examination and arthroscopic examination [21].

Commonly used conservative therapies for adhesive capsulitis include non-steroidal anti-inflammatory drugs, intra-articular glucocorticosteroid injections, oral glucocorticosteroid medication, physical therapy, manipulation under anaesthesia and hydrodilatation [22]. However, despite the amount of research in the topic, results still appear to be inconclusive regarding effectiveness of the different treatment modalities [23, 24]. In hydrodilatation or arthrographic distension procedures, an intra-articular injection is performed under fluoroscopy with local anaesthetics, normal saline and often with contrast medium. Most of the interventional studies with corticosteroid injections, with or without hydrodilatation (distension), have been done with single corticosteroid injection under fluoroscopy or ultrasound guided, either subacromial or intra-articular or both. Van der Windt et al. [25] used up to a maximum of three intra-articular injections over 6 weeks. According to Cyriax's treatment method [1], adhesive capsulitis is often treated with between three to six corticosteroid intra-articular injections with increasing interval between injections, which is also supported by others [4–6, 26]. A short term efficacy of arthrographic distension with normal saline and corticosteroid versus placebo was demonstrated in a randomised controlled trial (RCT) in patients with painful stiff shoulder [27]. A systematic Cochrane review regarding efficacy of hydrodilatation concludes: "there is "silver" level evidence that arthrographic distension with saline and steroid provides short-term benefits in pain, range of movement and function in adhesive capsulitis. It is uncertain whether this is better than alternative interventions" [28]. Hydrodilatation studies [29–31] did not demonstrate any statistically significant differences in functional outcome compared to steroid injection [32].

The present study has followed the existing practice of treating patients with adhesive capsulitis in primary care in Norway. In a pilot trial, there was no clinically significant difference in overall results between corticosteroid alone and corticosteroid with distension [33]. The aim of this study was to elucidate the effect, if any, of multiple corticosteroid injections with distension as compared to multiple corticosteroid injections alone, to treatment-as-usual.

Methods

This RCT comprises two parallel intervention groups and a control group allocating equal number of patients. The intervention period lasted 8 weeks, with a postal follow-up after 1 year. The patients were recruited from the city of Bergen and neighboring municipalities by referral from primary care (PC) practitioners from January 2010 to October 2013.

Included patients had to be above 18 years of age, should be able to understand and speak Norwegian, and have no contraindication for use of corticosteroids. Patients should have reduced passive range of motion (PROM) with a reduction of more than 30 % of two of three shoulder movements and none of the three movements (Abduction = ABD, External rotation = ER and Internal rotation = IR) should be normal. Patients with diabetes, asthma, pregnant women and breast feeding mothers were excluded from the study. Female patients in fertile age were asked about prevention.

Eligible patients were invited to participate in the study were randomly assigned to one of three groups according to serial no. on the closed envelope by one of authors (SPS). The block randomisation, using a block size of three, was carried out by one of the supervisors (AB). Possible permutations were strung together using a random cipher table. The resulting information on treatment was printed out and put in a closed envelope with the patient serial number outside. The envelope was to be opened after the inclusion of the patient. Treatment allocation was thereby "blinded" for both researcher and patient at the point of inclusion. The patients in the active intervention groups were not informed which treatment option (with or without distension) was carried out.

Intervention

Intra-articular injections were administered by landmarks using posterior approach thus preventing the patients from seeing the size of syringe used. This was to avoid possible bias as the patients might consider treatment with distension and corticosteroid to be superior to corticosteroid alone. The injections were administered by one of the authors (SPS) who is both a general practitioner and a physiotherapist at a primary care center in municipality of Bergen and has several years of experience in treating adhesive capsulitis by intra-articular injections both by landmarks and ultrasound guided.

Patients in the steroid alone group (IS) received Triamcinolone 20 mg injection, with Lidocaine 10 mg/ml 3 ml and a total of 4 ml solution. Those in the distension group (ISD) also received steroid and Lidocaine (Triamcinolone 20 mg, 3 ml Lidocaine), but with additional physiological Sodium chloride 9 mg/ml, comprising a total volume from 8 ml and upwards to 20 ml. Limiting factors for injected volume were difficulty in further injection and/or increasing pain during injection. Injection to IS and ISD groups were given after inclusion on day 1, after 7, 17, and 31 days from the start. Adherence to planned intervention was assessed continuously by one of the authors (SPS). Patients receiving treatment-as-usual (TAU) were informed about the possibilities of optional conservative treatment, such as physiotherapy or pain medication other than corticosteroid injections or per oral corticosteroid medication until 61 days after inclusion.

Outcome measures

The primary outcome was the Shoulder pain and disability index (SPADI), which measures a combination of pain and functional disability on a score from 0 to 100, a high score indicating more pain and disability [34]. The second outcome measure was pain intensity on average for the previous 7 days, measured on a 10-point Numerical pain rating scale (NPRS), where 0 meant no pain and 10 meant unbearable pain. PROM was measured in sideways elevation (abduction), internal rotation (by "Hand behind back" method) and external rotation. A plurimeter, found to be a reliable gravity inclinometer, was used as the measuring instrument for PROM [35–37]. PROM was measured, also on the normal side, on all visits. PROM was measured in supine lying position for external and internal rotation, and for abduction in standing. The endpoint was when the arm could not be moved more or the pain became unbearable. To avoid discrepancies in measurements due to affection of movements of thumb joints, the distance in Hand-behind-back was measured in centimeters between the styloid process of the radius to the posterior inferior iliac spine. PROM was measured by a research collaborator (a GP) being unaware which group the patients were randomised to. The assessor who took PROM had experience in use of the plurimeter, and had shown acceptable inter-tester reliability [37]. The assessor made entries of the PROM on a separate paper so that confidentiality was maintained from the treating doctor throughout the study.

The time intervals between the consecutive treatments were 1, 1½ and 2 weeks. The control group remained without treatment with corticosteroids in injection or tablet form until 61 days, but could use NSAIDs, Paracetamol or Codeine as needed. SPADI and NPRS were registered on the first visit, after 4 and 8 weeks. The 1 year follow-up for SPADI was only by postal communication.

Sample size

For SPADI, being the primary outcome measure, we considered an outcome of 20 % better or worse to be clinically significant. This represents a difference in score of 14 at the level of SPADI = 70. Others have considered a difference in score of ≥10 to represent clinically important change [34, 38]. In a previous study where SPADI was a primary outcome measure, the variance in SPADI was 19.8 [27]. Given $\alpha = 0.05$, we calculated the sample size to be 31 in each group to have an 80 % power to detect a difference in mean SPADI score of ≥14. With a 10 % drop out the number of patients required for the study to have the above mentioned power were calculated to be 34 in each group.

Statistical analysis

Differences in outcome between the groups were analyzed using repeated measure ANCOVA and regression based ANCOVA. In our analysis we have distinguished between short-term follow-up (4 and 8 weeks) and long-term follow-up (12 months). Since the 4 and 8 weeks data were not independent, we chose to analyze these data as multiple follow-up observations. This was done in a repeated measures ANCOVA model with 4 and 8 weeks

observations as repeated measures to capture the main effect of treatment between groups [39] (p.197), and with pretest as a covariate to adjust for baseline differences between subjects. Similarly, we analyzed the long-term follow-up data in another ANCOVA model using a regression procedure with the 12 months observations as dependent variable, group as a categorical independent variable and pretest as a covariate. In an additional/secondary analysis we added other independent variables (specified) to both ANCOVA models to control for possible confounding.

Effect size (ES) for mean change in SPADI was also calculated by subtracting post-test score (8 weeks and 12 months) from baseline in two groups, dividing it by the standard deviation (SD) of the change score:

$$Effect\ size = \frac{[Mean\ of\ intervention\ group] - [Mean\ of\ treatment-as-usual\ group]}{Standard\ Deviation}$$

An ES of 0.8 is considered large and of crucial practical or clinical importance, while an ES of 0.2 is considered to be small and without any practical or clinical importance [39].

We performed intention to treat (ITT) analysis [40], keeping patients in their original allocations on randomisation in accordance with ITT principles [41]. We had intervention data for all patients until 8 weeks except for missing data for two patients for 4 weeks and one patient for 8 weeks. One year follow-up data was lacking for six patients. Missing data were imputed following ITT principles.

Software package IBM SPSS Statistics 22 for Windows, was used for all statistical analyses.

We have followed the CONSORT (Consolidated Standards of Reporting Trials) 2010 guidelines for reporting of parallel group randomised trials. Figure 1 included in the manuscript has followed 2010 CONSORT Flow Diagram template. CONSORT 2010 Checklists for Randomised Trials, CONSORT extension for Abstracts Checklist and TIDieR (Template for Intervention Description and Replication) checklist files.

Results

Of the 216 patients referred for the study, 146 met the inclusion criteria, whereof 40 patients declined to participate for fear of coming in the TAU group and not receiving treatment immediately. Seventy patients were excluded as they were less affected than the specified criteria for reduced ROM or had diabetes. One hundred and six patients were randomised for participation. Thirty-six patients were allocated to the IS group, 34 patients to the ISD group, and 36 patients to TAU (Fig. 1). All completed the specified intervention until 8 weeks, and there were no dropouts, except for one in the IS group. After 1 year 100 patients (95 %) answered the postal questionnaire. One year follow up ended in December 2014. No interim analysis was carried out during the trial.

Patient characteristics

Baseline characteristics of all the included patients are displayed in Table 1. The three groups were comparable in their baseline regarding age, gender, mean duration of shoulder pain, concurrent neck pain, previously frozen shoulder, number of affected right side and dominant side and sick leaves. There were no statistically significant differences between the three groups regarding side affected, operated shoulder prior to adhesive capsulitis, trauma to shoulder (traumatic adhesive capsulitis), previous shoulder treatment, and smoking. There was a statistically significant difference in use of analgesics at baseline between the two intervention groups ($p < 0.05$), but not between the injection groups and TAU. Furthermore, 11 patients in the distension group had "trauma to shoulder" whereas the IS group had two and the TAU had three patients with previous trauma.

Intervention

Thirty-five patients in the IS group and 34 patients in the ISD group received four injections each within the time frame of 8 weeks. After the intervention period of 8 weeks, 12 patients (33 %) in the TAU group received additional treatment with intra-articular injections with corticosteroid and Lidocaine, same as in the IS group, for pain relief, and three were operated. During the 8 weeks after recruitment, 11 patients in the TAU group had received NSAIDs and/or pain killers as needed, and three patients had received acupuncture for pain relief.

All three groups showed clinically significant change in SPADI from baseline to 8 weeks (>14 points improvement), although both intervention groups had improved significantly more as compared to the TAU group at 8 weeks. Similarly, there was a significant improvement in NPRS at 8 weeks for both intervention groups, but less in the TAU group. Change in PROM for abduction was slightly better between the distension group (54° increased to 69°; i.e. 15° increase) and the TAU group (51° increased to 57°; i.e. 6° increase) at 8 weeks (Table 2).

Both intervention groups had equivalent ES concerning SPADI at 8 weeks (ES 1.2) and 12 months (ES 0.3 and 0.4) (Table 3). At 12 months, however, the change in the TAU group was as large as the change in the two intervention groups and no statistical significant difference was found in SPADI between the three groups, illustrated in Fig. 2.

Repeated measure ANCOVA for short-term and regression based ANCOVA for long-term revealed no statistically significant difference between the two intervention groups in SPADI, NPRS and PROM, neither at

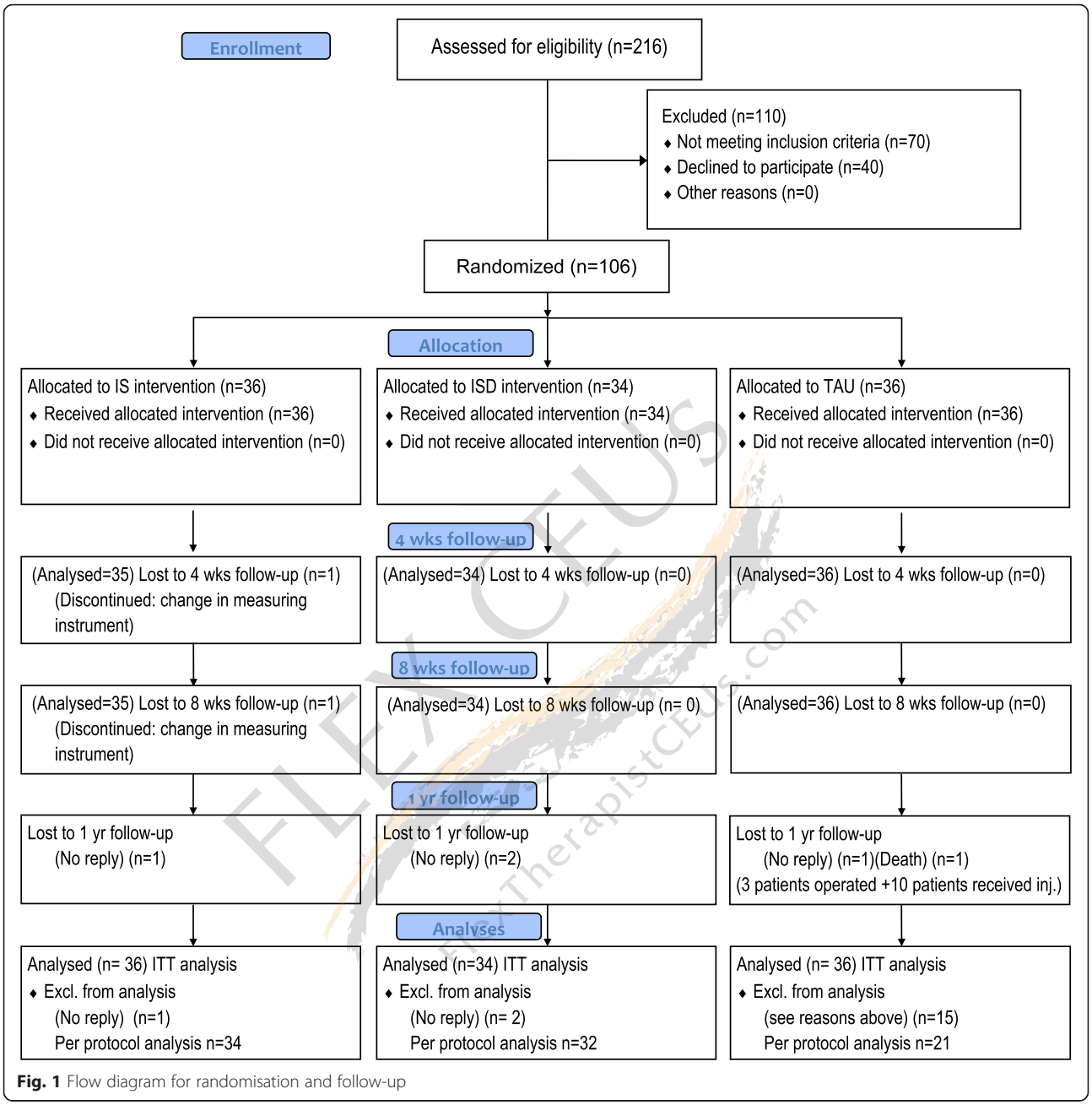

Fig. 1 Flow diagram for randomisation and follow-up

baseline, nor at short-term, or in SPADI at long-term. A statistically significant change (p <0.001) was found for both intervention groups when compared to the TAU group at short-term for SPADI and NPRS. There was a statistically significant difference ($p < 0.01$) at short-term for all PROMs between the two injection groups and TAU (Table 4).

In the TAU group, three patients were operated after 8 weeks, and 12 patients chose to receive intra-articular corticosteroid injections without distension. In the intention-to-treat analysis at 12 months, including all patients in the groups to which they were allocated, there were no significant differences between any of the groups regarding change in SPADI (Table 4).

In our study there was only one drop out up to 8 weeks and we did not expect this to affect the results substantially. A secondary per-protocol analysis was performed excluding the 15 patients that did not follow the initial TAU protocol after the 8 week period. This did not affect the results. However, we do acknowledge the fact that exclusion of these patients lowers the sample power for the TAU group.

Five patients (14 %) in the IS group, eight patients (24 %) in ISD group and six patients (14 %) in the TAU group were still on sick leave after 1 year. Eight patients

Table 1 Baseline characteristics of patients

Characteristics	Injection group Steroid alone (IS) Number and % within group $n = 36$	Injection group Steroid and saline (ISD) Number and % within group $n = 34$	Treatment-as-usual (TAU) group Number and % within group $n = 36$
Mean age (years)	52 (8.3)	53 (9.2)	54 (6.9)
Female	21 (58 %)	21 (62 %)	19 (53 %)
Duration in months Median (range)	7.5 (2.0–18.0)	7.0 (3.0–37.0)	6.0 (3.0–24.0)
Affected right shoulder	18 (50 %)	12 (35 %)	15 (42 %)
Previous frozen shoulder	6 (17 %)	4 (11 %)	4 (11 %)
Concurrent neck pain	16 (44 %)	15 (44 %)	16 (44 %)
Trauma to shoulder	2 (6 %)	11 (32 %)	3 (8 %)
Previous operation on shoulder	3 (8 %)	3 (9 %)	1 (3 %)
Dominant right side	34 (94 %)	30 (88 %)	34 (94 %)
Previous shoulder treatment	15 (42 %)	22 (65 %)	13 (36 %)
Analgesics	19 (53 %)	14 (41 %)	11 (31 %)
Participants on sick leave	17 (50 %)	16 (47 %)	15 (42 %)
Smokers	8 (22 %)	6 (18 %)	12 (33 %)

(22 %) in the IS group, nine patients (26 %) in the ISD group and three patients (8 %) in the TAU group were still on medication for shoulder pain at 12 months follow-up.

Six patients (17 %) in the IS group and four (12 %) patients in the ISD group experienced minor transitory side-effects such as flushing and after-pain. No incidences of other side effects were reported. Patients in the two injection groups were asked to guess to which group they belonged to after the last injection. Twenty-six patients (38 %) guessed the wrong group.

Discussion

Repeated intra-articular steroid injections given with increasing intervals in the gleno-humeral joint gives short-term (8 weeks) benefit. Added capsular distension did not significantly affect the outcome measures for SPADI, NPRS and PROM. However, at long-term follow-up, those who had received no intervention did equally well.

Earlier studies combining distension (10 ml) and corticosteroid versus distension alone and corticosteroid alone, have reported better results for distension [42]. While in studies by Corbeil et al. & Tveitå et al. [30, 31] no significant differences between distension and non–distension arthrography with corticosteroids were found, the main effect might therefore be attributed to corticosteroid alone. Comparing our results between ISD group and TAU group with Tveitå et al. [31], our study has demonstrated larger improvement; for SPADI 24 versus 6, for ABD 15.4 versus 2, for ER 18.7 versus 2 and for IR 12.3 versus 3 respectively. A systematic review concluded with "silver level" evidence for short–term efficacy in pain, ROM, and function of shoulder by arthrographic saline distension and corticosteroid in patients with adhesive capsulitis [28]. Studies with distension and corticosteroid causing capsular rupture performed in hospital settings have also shown significant results [27, 29, 42]. These and other case series studies in primary care with distension and capsular rupture [43, 44] are, however, not comparable to the present study, as capsular rupture was not the intended intervention. We cannot however rule out that capsular rupture might have occurred in some patients. Tveitå et al. [31] have observed capsular rupture at a volume as low as 10 ml.

A dose of 20 mg Triamcinolone was a tradeoff dose between effect and side effects in both intervention groups and is the generally accepted and practiced treatment dose for adhesive capsulitis in primary care. A study by de Jong [45] has shown better effect with a dose of 40 mg Triamcinolone than with 10 mg, whereas another study by Yoon et al. [46] found no significant difference in outcome between a dose of 20 and 40 mg Triamcinolone. In this study we used a series of injections, a total of four over a period of 8 weeks. Many studies with distension have only used a single corticosteroid injection, which makes comparison difficult. Only a few studies have used multiple injections and even fewer have used multiple injections with dilatation [25, 29, 31, 42, 47]. A review has concluded that multiple injections improve pain and ROM in short term from 6 to 16 weeks from the first injection. There is evidence that up to three injections can be beneficial and limited evidence that up to six injections is beneficial [4].

This study has followed the actual practice of treating these patients in primary care with intra-articular injections by landmarks, without fluoroscopic guidance. Some studies with ultrasound guided intra-articular steroid

Table 2 SPADI, NPRS and PROM and comparison in outcomes between three groups

	Injection group Steroid alone (IS) Mean (SD)	Injection group Steroid and saline (ISD) Mean (SD)	Treatment-as-usual (TAU) Mean (SD)
Primary outcome variable			
SPADI			
At inclusion	63.8 (16.0)	60.5 (16.8)	61.9 (19.0)
4 weeks	34.1 (21.4)	30.9 (21.0)	51.9 (22.2)
8 weeks	23.8 (22.0)	20.1 (18.4)	44.4 (23.6)
12 months	16.9 (18.9)	17.2 (19.8)	11.7 (20.3)
Secondary outcome variable			
NPRS			
At inclusion	6.9 (1.4)	7.2 (1.6)	6.6 (2.1)
4 weeks	3.8 (2.2)	3.5 (1.7)	5.6 (2.5)
8 weeks	3.0 (2.3)	2.9 (1.6)	4.7 (2.0)
Tertiary outcome variables			
Abduction (ABD)			
At inclusion	53.7 (13.4)	51.0 (17.8)	50.5 (19.0)
4 weeks	62.7 (15.6)	64.7 (17.2)	53.9 (19.4)
8 weeks	68.9 (15.3)	71.9 (17.0)	56.5 (20.9)
External rotation (ER)			
At inclusion	19.6 (14.7)	25.2 (17.7)	17.3 (13.5)
4 weeks	30.1 (16.3)	35.6 (15.8)	18.8 (14.8)
8 weeks	38.2 (17.6)	42.7 (17.9)	24.0 (18.1)
Internal rotation (IR)			
At inclusion	38.8 (15.5)	41.1 (14.1)	40.2 (15.4)
4 weeks	49.5 (17.4)	52.7 (17.3)	43.7 (16.6)
8 weeks	57.2 (15.7)	59.6 (16.1)	47.3 (18.2)
Hand behind back (HBB)			
At inclusion	0.4 (6.2)	2.2 (7.8)	−0.5 (6.0)
4 weeks	5.9 (7.2)	7.5 (7.8)	1.0 (6.1)
8 weeks	10.1 (6.3)	11.2 (7.2)	4.3 (6.5)

SPADI shoulder pain and disability index, *NPRS* numeric pain rating scale, *PROM* passive range of motion
IS injection steroid alone, *ISD* injection steroid plus saline, *TAU* treatment-as-usual

Table 3 Effect size (ES) for SPADI from baseline to 8 weeks and 12 months follow-up for the three groups

SPADI	IS	ISD	TAU	IS & ISD	IS & TAU	ISD & TAU
8 weeks						
Mean change	−40.3	−40.4	−17.4	0.2	22.8	23.0
SD	19.0	19.1	19.8	19.1	19.4	19.4
ES				0.0	1.2	1.2
12 months						
Mean change	−43.0	−39.8	−48.1	3.1	5.1	8.2
SD	19.6	24.7	20.4	22.3	20.0	21.4
ES				0.1	0.3	0.4

SPADI shoulder pain and disability index
IS injection steroid alone, *ISD* injection steroid plus saline, *TAU* treatment-as-usual

injections claim a short time superiority in pain reduction of about 2 weeks, compared to injections by landmarks [48], which we consider is little as compared to the extra resources required in terms of time and costs.

On 1 year follow-up all three groups had similar outcome, which reflects the natural history of the condition [14, 16, 18, 20, 49]. But the major difference in pain relief (NPRS) and pain and function (SPADI) were recorded in the first 8 weeks in the intervention groups as compared to the control group. From the patient's perspective, pain relief leading to undisturbed sleep is of great importance [50], which is not so often accredited in studies measuring outcome over time.

One of the strengths of this study is that it is conducted in line with the actual practice in treatment of

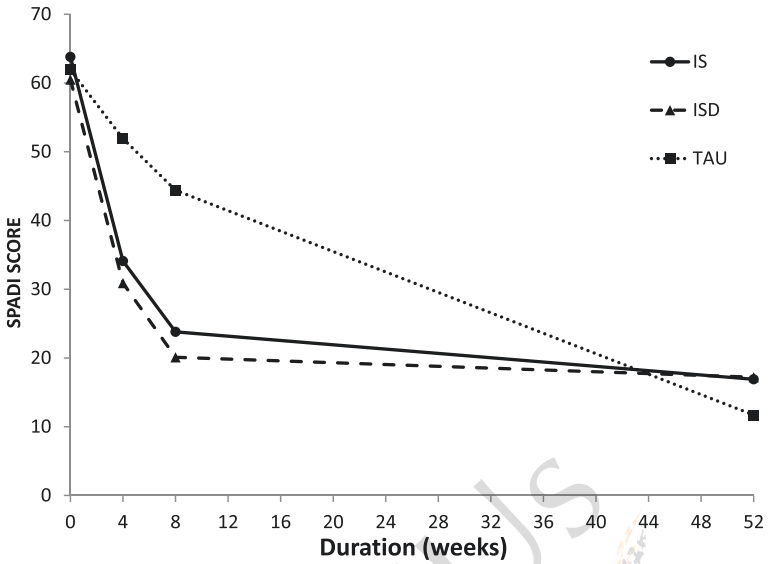

Fig. 2 Comparison between intervention and treatment-as-usual groups from inclusion to 52 weeks for SPADI

adhesive shoulder capsulitis in primary care in Norway, i.e. intra-articular steroid injection in gleno-humeral joint by landmarks. There are very few studies that are close to actual practice in treatment of shoulder adhesive capsulitis in primary care [25, 51]. The procedure is safe and simple and easy to learn and cost effective. Only 15 % of patients reported transient side effects and the procedure was not experienced as particularly painful. The limitations of the study are lack of visual verification of delivery of medication in the joint. The injected volume varied from 8 to 20 ml and we cannot assert with certainty that the observed

Table 4 SPADI, NPRS and PROM: Differences in change scores between the two injection groups (Intervention steroid alone (IS); Intervention steroid plus saline (ISD)) and the treatment-as-usual group (TAU)

	Between groups differences in change, mean (95 % CI)		
	IS vs ISD	IS vs TAU	ISD vs TAU
Primary outcome variable			
SPADI			
Short-term (4 and 8 weeks)[a]	1.2 (−7.1 to 9.6)	−20.8 (−28.9 to −12.7)***	−21.7 (−29.4 to −14.0)***
Long-term (12 months)[b]	0.1 (−10.4 to 10.7)	−7.0 (−16.4 to 2.5)	−7.0 (−16.8 to 2.8)
Secondary outcome variable			
NPRS			
Short-term (4 and 8 weeks)[a]	0.3 (0.6 to 1.2)	−2.0 (−2.8 to −1.1)***	−2.2 (−3.0 to −1.4)***
Tertiary outcome variables			
Abduction			
Short term (4 and 8 weeks)[a]	−4.5 (−9.7 to 0.8)	8.3 (2.3 to 14.3)**	12.7 (6.6 to 18.9)***
External rotation			
Short term (4 and 8 weeks)[a]	−0.9 (−5.8 to 4.1)	10.8 (5.8 to 15.9)***	11.9 (6.8 to 17)***
Internal rotation			
Short term (4 and 8 weeks)[a]	−1.1 (−6.6 to 4.5)	8.8 (3.1 to 14.6)**	9.9 (4.7 to 15.1)***
Hand behind back			
Short term (4 and 8 weeks)[a]	−0.7 (−2.4 to 2.2)	5.0 (2.8 to 7.2)***	5.1 (2.9 to 7.2)***

SPADI shoulder pain and disability index, *NPRS* numeric pain rating scale, *PROM* passive range of motion
***$p < 0.001$, **$p < 0.01$, *$p < 0.05$
[a]Repeated measures ANCOVA with baseline value as covariate. Differences and CIs from estimated marginal means
[b]Regression based ANCOVA with baseline value as covariate

effect was due to distension and not to capsular rupture. Longer time taken in injecting the fluid in the joint might have introduced bias as patients might as-
sume that he or she was in the distension group, which might have been considered the superior method by the patients.

Conclusion

This intention to treat RCT in primary care indicates that four injections with corticosteroid with or without distension, given with increasing intervals during 8 weeks, were better than treatment-as-usual in adhesive capsulitis of the shoulder. However, in the long run no difference was found between any of the groups, indicating that natural healing takes place independent of treatment.

Acknowledgements

Sincere thanks to Nils Ivar Aanes M.D. for being the "blinded" tester, Shruti Sharma M.D. for data entry and calculations of SPADI and for helping in postal follow-up. This study was supported by the General Practice Research Fund of The Norwegian Medical Association. A grant was also received from Dr. Trygve Gythfeldt and wife's research fund which covered additional expenditure for example purchase of drugs and payments to assessors.

Competing interests

The authors declare that they have no competing interests.

References

1. Cyriax J. Textbook of Orthopaedic Medicine. Diagnosis of Soft Tissue lesions, vol. 2. 7th ed. London: Baillie're Tindall; 1982.
2. Lorbach O, Anagnostakos K, Scherf C, Seil R, Kohn D, Pape D. Nonoperative management of adhesive capsulitis of the shoulder: oral cortisone application versus intra-articular cortisone injections. J Shoulder Elbow Surg. 2010;19(2):172–9.
3. Lundberg BJ. Arthrography and Manipulation in Rigidity of the Shoulder Joint. Acta Orthop Scand. 1965;36:35–44.
4. Shah N, Lewis M. Shoulder adhesive capsulitis: systematic review of randomised trials using multiple corticosteroid injections. Br J Gen Pract. 2007;57(541):662–7.
5. Ombregt L, Bisschop P, Veer HJ, Van de Velde T. A System of orthopaedic medicine. London: Saunders; 1995.
6. Kesson M, Atkins E. Orthopaedic medicine: a practical approach. Oxford: Butterworth-Heinemann; 1998.
7. Buchbinder R, Green S. Effect of arthrographic shoulder joint distension with saline and corticosteroid for adhesive capsulitis. Br J Sports Med. 2004;38(4):384–5.
8. Dias R, Cutts S, Massoud S. Frozen shoulder. BMJ. 2005;331:1453–6.
9. Neviaser TJ. Adhesive capsulitis. Orthop Clin North Am. 1987;18(3):439–43.
10. Hsu JE, Anakwenze OA, Warrender WJ, Abboud JA. Current review of adhesive capsulitis. J Shoulder Elbow Surg. 2011;20(3):502–14.
11. Nagy MT, Macfarlane RJ, Khan Y, Waseem M. The frozen shoulder: myths and realities. Open Orthop J. 2013;7:352–5.
12. Wiley AM. Arthroscopic appearance of frozen shoulder. Arthroscopy. 1991; 7(2):138–43.
13. Bunker TD, Anthony PP. The pathology of frozen shoulder. A Dupuytren-like disease. J Bone Joint Surg (Br). 1995;77:677–83.
14. Grey RG. The natural history of "idiopathic" frozen shoulder. J Bone Joint Surg Am. 1978;60(4):564.
15. Miller MD, Wirth MA, Rockwood Jr CA. Thawing the frozen shoulder: the "patient" patient. Orthopedics. 1996;19(10):849–53.
16. Binder AI, Bulgen DY, Hazleman BL, Roberts S. Frozen shoulder: a long-term prospective study. Ann Rheum Dis. 1984;43(3):361–4.
17. Hand C, Clipsham K, Rees JL, Carr AJ. Long-term outcome of frozen shoulder. J Shoulder Elbow Surg. 2008;17(2):231–6.
18. Shaffer B, Tibone JE, Kerlan RK. Frozen shoulder. A long-term follow-up. J Bone Joint Surg Am. 1992;74:738–46.
19. Hannafin JA, Chiaia TA. Adhesive capsulitis. A treatment approach. Clin Orthop Relat Res. 2000;372:95–109.
20. Reeves B. The natural history of the frozen shoulder syndrome. Scand J Rheumatol. 1975;4(4):193–6.
21. Neviaser AS, Hannafin JA. Adhesive Capsulitis. Am J Sports Med. 2010;38(11): 2346–56.
22. Griesser MJ, Harris JD, Campbell JE, Jones GL. Adhesive Capsulitis of the Shoulder: a systematic review of the effectiveness of intra-articular corticosteroid injections. J Bone Joint Surg Am. 2011;93:1727–33.
23. Blanchard V, Barr S, Cerisola FL. The effectiveness of corticosteroid injections compared with physiotherapeutic interventions for adhesive capsulitis: a systematic review. Physiotherapy. 2010;96(2):95–107.
24. Green S, Buchbinder R, Glazier R, Forbes A. Systematic review of randomised controlled trials of interventions for painful shoulder: selection criteria, outcome assessment, and efficacy. BMJ. 1998;316(7128):354–60.
25. van der Windt DA, Koes BW, Deville W, Boeke AJ, de Jong BA, Bouter LM. Effectiveness of corticosteroid injections versus physiotherapy for treatment of painful stiff shoulder in primary care: randomised trial. BMJ. 1998; 317(7168):1292–6.
26. Siegel LB, Cohen NJ, Gall EP. Adhesive capsulitis: a sticky issue. Am Fam Physician. 1999;59(7):1843–52.
27. Buchbinder R, Green S, Forbes A, Hall S, Lawler G. Arthrographic joint distension with saline and steroid improves function and reduces pain in patients with painful stiff shoulder: results of a randomised, double blind, placebo controlled trial. Ann Rheum Dis. 2004;63(3):302–9.
28. Buchbinder R, Green S, Youd JM, Johnston RV, Cumpston M. Arthrographic distension for adhesive capsulitis (frozen shoulder). Cochrane Database Syst Rev. 2008;1:CD007005.
29. Gam AN, Schydlowsky P, Rossel I, Remvig L, Jensen EM. Treatment of "frozen shoulder" with distension and glucorticoid compared with glucorticoid alone. A randomised controlled trial. Scand J Rheumatol. 1998; 27(6):425–30.
30. Corbeil V, Dussault RG, Leduc BE, Fleury J. [Adhesive capsulitis of the shoulder: a comparative study of arthrography with intra-articular corticotherapy and with or without capsular distension]. Can Assoc Radiol J. 1992;43(2):127–30.

31. Tveita EK, Tariq R, Sesseng S, Juel NG, Bautz-Holter E. Hydrodilatation, corticosteroids and adhesive capsulitis: a randomized controlled trial. BMC Musculoskelet Disord. 2008;9:53.
32. Uppal HS, Evans JP, Smith C. Frozen shoulder: A systematic review of therapeutic options. World J Orthop. 2015;6(2):263–8.
33. Sharma S, Kvåle A, Bærheim A. Outcome in shoulder capsulitis (frozen shoulder) treated with corticosteroid and corticosteroid with distension - a randomised pilot study. Int Musculoskelet Med. 2009;3:5.
34. Williams Jr JW, Holleman Jr DR, Simel DL. Measuring shoulder function with the Shoulder Pain and Disability Index. J Rheumatol. 1995;22(4):727–32.
35. Green S, Buchbinder R, Forbes A, Bellamy N. A standardized protocol for measurement of range of movement of the shoulder using the Plurimeter-V inclinometer and assessment of its intrarater and interrater reliability. Arthritis Care Res. 1998;11:43–52.
36. Hoving JL, Buchbinder R, Green S, Forbes A, Bellamy N, Brand C, Buchanan R, Hall S, Patrick M, Ryan P, et al. How reliably do rheumatologists measure shoulder movement? Ann Rheum Dis. 2002;61:612–6.
37. Sharma SP, Baerheim A, Kvale A. Passive range of motion in patients with adhesive shoulder capsulitis, an intertester reliability study over eight weeks. BMC Musculoskelet Disord. 2015;16:37.
38. Carette S, Moffet H, Tardif J, Bessette L, Morin F, Fremont P, Bykerk V, Thorne C, Bell M, Bensen W, et al. Intraarticular corticosteroids, supervised physiotherapy, or a combination of the two in the treatment of adhesive capsulitis of the shoulder: a placebo-controlled trial. Arthritis Rheum. 2003;48(3):829–38.
39. Norman GR, Streiner DL. Biostatistics The Bare Essentials. 4th ed. Shelton: People's Medical Publishing House-USA; 2014.
40. Lewis JA, Machin D. Intention to treat–who should use ITT? Br J Cancer. 1993;68(4):647–50.
41. Abraha I, Cherubini A, Cozzolino F, De Florio R, Luchetta ML, Rimland JM, Folletti I, Marchesi M, Germani A, Orso M, et al. Deviation from intention to treat analysis in randomised trials and treatment effect estimates: meta-epidemiological study. BMJ. 2015;350:h2445.
42. Jacobs LG, Barton MA, Wallace WA, Ferrousis J, Dunn NA, Bossingham DH. Intra-articular distension and steroids in the management of capsulitis of the shoulder. BMJ. 1991;302(6791):1498–501.
43. Fareed DO, Gallivan Jr WR. Office management of frozen shoulder syndrome. Treatment with hydraulic distension under local anesthesia. Clin Orthop Relat Res. 1989;242:177–83.
44. Halverson L, Maas R. Shoulder joint capsule distension (hydroplasty): a case series of patients with "frozen shoulders" treated in a primary care office. J Fam Pract. 2002;51(1):61–3.
45. de Jong BA, Dahmen R, Hogeweg JA, Marti RK. Intra-articular triamcinolone acetonide injection in patients with capsulitis of the shoulder: a comparative study of two dose regimens. Clin Rehabil. 1998;12(3):211–5.
46. Yoon SH, Lee HY, Lee HJ, Kwack KS. Optimal Dose of Intra-articular Corticosteroids for Adhesive Capsulitis A Randomized, Triple-Blind, Placebo-Controlled Trial. Am J Sports Med. 2013;41(5):1133–9.
47. Piotte F, Gravel D, Moffet H, Fliszar E, Roy A, Nadeau S, Bedard D, Roy G. Effects of repeated distension arthrographies combined with a home exercise program among adults with idiopathic adhesive capsulitis of the shoulder. Am J Phys Med Rehabil. 2004;83(7):537–46. quiz 547-539.
48. Lee H-J, Lim K-B, Kim D-Y, Lee K-T. Randomized Controlled Trial for Efficacy of Intra-Articular Injection for Adhesive Capsulitis: Ultrasonography-Guided Versus Blind Technique. Arch Phys Med Rehabil. 2009;90(12):1997–2002.
49. Vastamäki HMD, Kettunen JPTP, Vastamäki MMDP. The Natural History of Idiopathic Frozen Shoulder: A 2- to 27-year Followup Study. Clin Orthop Relat Res. 2012;470(4):1133–43.
50. Smith CD, Hamer P, Bunker TD. Arthroscopic capsular release for idiopathic frozen shoulder with intra-articular injection and a controlled manipulation. Ann R Coll Surg Engl. 2014;96(1):55–60.
51. Winters JC, Sobel JS, Groenier KH, Arendzen HJ, Meyboom-de Jong B. Comparison of physiotherapy, manipulation, and corticosteroid injection for treating shoulder complaints in general practice: randomised, single blind study. BMJ. 1997;314:1320.

Suprascapular Nerve Block Followed by Codman's Manipulation and Home Exercises "An Effective Combined Approach in the Rehabilitation of Idiopathic Frozen Shoulder": A Review

Abstract

Frozen shoulder is characterized by inflammation of the synovial lining and capsule, with subsequent generalized contracture of the glenohumeral joint causing shoulder pain and a gradual loss of both passive and active range of motion. The pathology of idiopathic frozen shoulder is defined as a self-limiting condition of unknown etiology. Pain relief through suprascapular nerve block (SSNB) followed by manipulation and home exercises may be a suitable treatment option in such patients.

Keywords: Adhesive capsulitis; Codman's manipulation; Frozen shoulder; Manipulation; Suprascapular nerve block

Introduction

The term "frozen shoulder" was first used by Codman [1] and thereafter Neviaser [2] noted that the pathology of the condition was actually located at the capsule of the shoulder joint and therefore called it "adhesive capsulitis". The typical findings are pain and a global restriction of movement, with limited passive external rotation being the most notable [3]. Frozen shoulder management presents the clinicians with an opportunity to use all skills to alleviate pain and restore function of the shoulder.

Many treatment options for adhesive capsulitis have been described, including rest, NSAIDs, active and passive mobilization, physiotherapy, intra-articular corticosteroids, intra-articular hyaluronate injection, manipulation under anaesthesia when conservative treatment fails, and finally arthroscopic capsular release [4-7]. One of the main goals of treatment is to restore shoulder function through manipulation and therapeutic exercises in which the patient must cooperate and take an active part. The most important factor limiting patients' cooperation in exercise is pain. Hence, regional nerve block, attributable to its role in pain relief, can be used before the exercise program [8]. Among various nerve block techniques, suprascapular nerve block (SSNB) is an effective and simple method for the management of shoulder pain, with no significant complications reported in over 2000 procedures apart from rare vasovagal episodes [9-12].

Although frozen shoulder is believed to be a benign self-limiting disorder, which tends to be resolved over 1-2 years, authors suggested that patients with significant stiffness are good candidates for manipulation under anaesthesia rather than conventional treatment because conventional treatment of intensive physiotherapy must be carried out for months to years in order to regain the range of motion (ROM) [13,14].

It must be emphasized that even after manipulation of shoulder, a regular supervised physiotherapy is critical to ensure a mobile painless shoulder otherwise significant stiffness quickly return. Multiple shoulder manipulation techniques have been described, including manipulation with steroid injection and manipulation under general or local anaesthesia. Fracturing the humerus during shoulder manipulation is a common complication, in addition to shoulder dislocation, post-manipulation pain, hemoarthrosis, tearing of the joint capsule or rotator cuff, and traction injury to nerves [15].

The Codman's manipulation refers to a specific pattern of motion at the shoulder joint leading to an indirect humeral rotation without placing a rotational torque on the humerus, thereby reducing fracture risk during manipulation. This is achieved when the arm performs a closed-loop motion by three consecutive 90° rotations defined as Codman's rotations, each around the respective coordinate axis. Such rotations will lead to an apparently indirect 90° rotation around the longitudinal axis of the humerus [16,17].

Epidemiology

The prevalence of adhesive capsulitis is 2-5% in a normal population [18,19]. It is more common in females and between the ages of 40 and 60 years [1,20]. A genetic component is reported although the direct mechanisms by which genes influence soft tissue disorders are still unknown [21]. Contra lateral shoulder involvement shoulder involvement reported in up to 20-30% of patients and recurrence in ipsilateral shoulder is unusual [18].

Natural history

The natural history of idiopathic frozen shoulder syndrome is considered benign. Codman [1] and Grey [22] stated that frozen shoulder is a self-limiting condition with complete resolution of pain and recovery of range of motion within a maximum of 2 years from the onset of symptoms.

Deplama [23] reported on three patients who had remained symptomatic five, six and eight years after the onset of symptoms with no indication of improvement.

Murnaghan [24] stated that "the time course of return of shoulder motion is quite unpredictable". The long period of pain and disability reported in cases of frozen shoulder has been the reason for different interventions management.

Pathology of "frozen shoulder"

The pathophysiological process is believed to involve synovial inflammation and fibrosis of the shoulder joint capsule [25]. Cytokines such as Transforming Growth Factor-beta (TGF-β) and Platelet Derived Growth Factor (PDGF) may contribute to the inflammatory process [26]. Hand et al. found a chronic inflammatory response with a chronic inflammatory response with a fibroblastic proliferation suggesting the process to be immunomodulated [25].

Four arthroscopic stages described by Naviaser as inflammatory, freezing, frozen, and thawing [2]. In the inflammatory stage, passive ROM is increased with anaesthesia, indicating that ROM is pain limited. Histologically, there are inflammatory infiltrates and hypervascular synovitis with a normal underlying capsule. The freezing stage differs in that passive ROM is similar with or without anaesthesia and histologically shows hypertrophic, hypervascular synovitis with capsular scaring. In the frozen stage, pathological specimens show reduced synovitis and dense scar formation in the underlying capsule. The thawing stage represents resolution and no pathological specimens have been described [27,28]. On the contrary Lundberg [29] documented periarticular inflammatory changes and thickening of the joint capsule without intra-articular adhesions. Rizk et al. [30] discovered thickening and constriction of the capsule. Ozaki [31] found a contracted and hypertrophied coracohumeral ligament.

Clinical Picture

The diagnosis is made on the basis of medical history and clinical examination. In 1934 Codman [1] proposed the following diagnostic criteria for frozen shoulder:

- Shoulder pain of slow onset.
- Pain felt at the deltoid insertion.
- Inability to sleep on affected side.
- Atrophy of supra- and infra spinatus muscles.
- Restriction of active and passive ROM.
- Painful and restricted elevation and external rotation.

History

Most patients with idiopathic frozen shoulder have no history of shoulder trauma. They usually give a history of insidious onset of pain, followed by a loss of motion. Night and rest pain are common in the early stages.

Clinical examination

The only sign found in the early stages of the disease process is pain experienced at the end range of shoulder motion. Patients presenting with inflammatory and freezing stages have pain on palpation of the anterior and posterior capsule and describe pain radiating to the deltoid insertion. Later on in the disease process, a mild disuse atrophy of the deltoid and supraspinatus muscles can be found. A diffuse tenderness with palpation over the glenohumeral joint can extend to the trapezius and interscapular area [4]. It has been found that complete loss of external rotation is pathognomonic for frozen shoulder [32]. The disease process least affects extension and horizontal adduction movements [33]. Most of the movements in a severely affected frozen shoulder occur at the scapula-thoracic joint.

Special examinations

Plain x-rays mostly reported as normal but some may show periarticular osteopenia due to disuse [34]. These x-rays can assist in excluding other causes of stiff shoulder, such as rotator cuff disease and glenohumeral arthritis [35]. MRI can be helpful in identifying other causes of a stiff shoulder, such as infection or tumors. Laboratory investigations are useful in patients with other medical issues that may lead to secondary frozen shoulder. These include fasting blood glucose, lipid profile and thyroid stimulating hormone.

Management of frozen shoulder

The decision regarding the best treatment option must be individualized to each patient depending on the stage of the disease and clinical symptoms, as there is no consensus on a standard management protocol.

Non-surgical treatment

Medications

Oral non-steroidal anti-inflammatory drugs can be initiated in patients who present with painful limited ROM during the painful freezing phase [6]. Oral steroids have been proposed as a treatment option for frozen shoulder [7]. However, Bushbinder et al. [36] found that, although it did improve the symptoms initially, the effect did not last beyond six weeks. In light of its adverse reactions, some authors suggest that it should not be routinely used for this condition.

Intra-articular steroids

A corticosteroid intra-articular injection has been extensively used in different ways and with different success rates ranging from 44 to 80% [30,37]. A cochrane database review showed that it might be beneficial in the short term and that the effect will not maintained [38]. However, it is more effective when used in combination with other therapies. Carrette et al. [39] found that intra-articular steroids combined with physiotherapy were more effective in improving shoulder ROM than when each of these was used individually. Jacobs et al. [40] also showed that a combination of steroids and distension had the same outcome at two years as manipulation under anaesthesia.

Physiotherapy

Physiotherapy alone is an effective treatment but is a complement to other therapies, especially to improve the range of movement in external rotation [41,42]. The goal should be to stretch the capsule sufficiently to allow normal glenohumeral biomechanics. Diercks et al. [41] compared the outcome of 77 patients after some received intensive physiotherapy (passive stretching and manual mobilization) and other supervised neglect (active exercises within pain-free range and

pendulum exercises). The supervised –neglect group showed the best results with 89% of patients' having normal painless shoulders compared to the intensive group with only 63% of patients achieving the same results.

Hydrodilation

Hydrodilation was first described by Andren and Lundberg [43] in 1965, appears to be another good therapeutic intervention for achieving rapid symptomatic relief from adhesive capsulitis [44,45]. It consists of an injection of a solution causing rupture of the capsule by hydrostatic pressure. The solution could be saline solution or combined with corticosteroids [45]. Quraishi et al. [46] showed better results with hydrodilation than manipulation under anaesthesia. They reported that at 6 months follow-up the Constant score showed a statistically significant improvement. However, the ROM had not improved.

Surgical treatment

Manipulation under anaesthesia

Duplay [47] initially recommended this kind of manipulation as a treatment option for adhesive capsulitis in 1872. It is generally indicated in patients with persistent functional disability in spite of adequate non-operative treatment for 4-6 months. However, opponents cite the risk for dislocation, fracture, nerve palsy, and rotator cuff tears as limitations to this technique [15]. During this procedure, the synovium, the joint capsule especially the inferior axillary pouch of capsule are ruptured, but tears have also been observed to involve the intra-articular long head of biceps and the subscapularis tendon [48]. Some authors [35,49] recommend that an arthroscopic examination be performed before a closed manipulation as they have shown that it helps to reduce stiffness and pain. Physiotherapy is recommended for two to six weeks post-surgery.

Arthroscopic capsular release

The first arthroscopic release was described by Conti in 1979. It is especially recommended in diabetic patients or in patients with post-operative or post-fracture frozen shoulder [50]. Arthroscopy has been considered useful to confirm the diagnosis, to exclude other significant pathology, to classify the stage of the disease and to treat the stiff shoulder with or without manipulation [51]. Potential risks of arthroscopic capsular release include recurrent stiffness, post-operative anterior dislocation and axillary nerve injury at the 6 o'clock position [3]. Pain pumps are suggested to assist in early pain-free mobilization in the first few days. These should be placed in the subacromial space; as some complications have been reported if placed intra-articular [3]. Patients can be started on physiotherapy in hospital and discharged on home exercises that are both passive and active-assisted. Continuous passive motion (CPM) can be helpful in refractory cases [3].

Open surgical release

Open surgical release should be considered in patients for whom arthroscopy is contraindicated or has failed [51]. Traditionally, non-operative management of adhesive capsulitis is recommended for a minimum of six to twelve months before considering operative intervention [52]. However, patients with persistent symptoms and those who have risk factors such as diabetes mellitus or are affected bilaterally might benefit from earlier surgical [53].

SSNB and Codman's manipulation Therapies

Anatomical background

The shoulder joint is supplied primarily by axillary nerve and suprascapular nerve with small branches from the subscapular and lateral pectoral nerves. SSN originates from the upper trunk with contribution from C5-6 and some variable contribution from C4. It travels anterior to the trapezius and parallel to omohyoid, crosses the posterior triangle to enter the suprascapular notch. The superior articular branch comes off 4.5 cm proximal to transverse scapular ligament and continues along with the main nerve beneath the ligament [54]. The SSN then travels towards the spine where it sends a branch to the supraspinatus muscle and winds around the spinoglenoid notch to supply the infraspinatus muscle. In its course along the scapular spine, the inferior articular branch separates from the main nerve and courses obliquely to supply the posterior shoulder joint [55]. SSN supplies 70% of the sensory fibers to the superior and postero-superior shoulder joint, the acromio- clavicular joint, capsule and overlying skin variably [56].

Techniques

Suprascapular nerve block techniques

Traditionally, SSN blockade has been performed via the use of anatomical landmarks. More recently, the use of imaging guidance to more accurately guide needle placement has been described [56]. Various landmark approaches have been described and can be categorized into posterior, superior and lateral approaches. The posterior approach attempts to block the SSN at the level of suprascapular notch [57-61], while the superior approach aims to block the SSN by surrounding the nerve with local anaesthetic on the floor of supraspinous fossa [62,63]. A lateral approach to localize the SSN has also been described [64,65]. Disadvantages of the posterior approach are the potential absence of suprascapular notch in some individuals and the potential risk of pneumothorax. The superior approach may negate these disadvantages. Dangoisse et al. described an indirect SSN block, using anatomical landmarks [63]. This type of approach is easy and decreases the risk of pneumothorax. It can be performed by most trained specialists.

Dangoisse technique

A 25-G needle has to be introduced through the skin 2 cm cephaloid to the midpoint of the spine of the scapula, with the patient sitting and the upper limbs bending beside the body. Anatomic landmarks must be palpated, such as clavicle, acromioclavicular articulation, acromion, scapular spine, and coracoid process. The entire area must be sterilized with alcohol, and then the needle to be advanced parallel to the blade of the scapula until bony contact is made in the floor of the suprascapular fossa (Figure 1). The needle must be aspired before infusion of anaesthetic solution so that there is no risk this solution enters the blood stream directly. This technique has previously been demonstrated to be safe, and it effectively blocks the articular branches of the suprascapular nerve [63]. For treatment of chronic shoulder conditions, injectable steroids usually are added to the local anaesthetic solution (10 ml solution of 0.5% bupivacaine

hydrochloride and 40 mg of methyl prednisolone acetate) [65-70]. Local steroid injection blocks transmission through nociceptive C fibers, thus prolonging the effect of the local anaesthetic through alteration of the function of K channel on the excitable tissue [71,72].

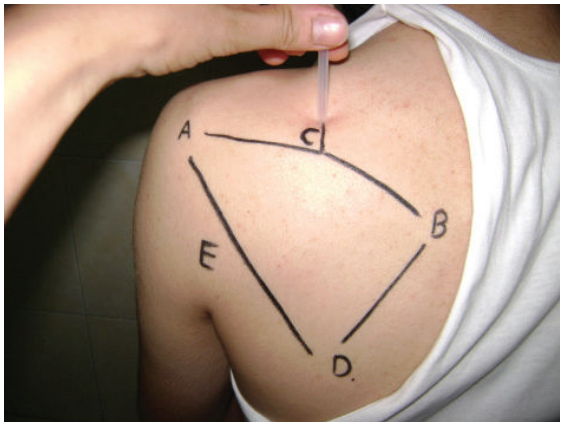

Figure 1: Posterior view of the suprascapular nerve block using the Dangoisse technique. Landmarks are indicated as follows: acromion and lateral end of the scapular spine (a), medial end of the scapular spine (b), midpoint of the scapular spine (c), inferior angle of the scapula (d), and lateral border of the scapula (e). The needle is aligned 2 cm superior to the midpoint of the scapular spine parallel to the blade of the scapula.

Complications

SSNB is a safe procedure with a generally low rate of complications. The largest study retrospectively analyzed 1,005 SSNBs performed by multiple clinicians in multiple centers over a 6-year period reported no major complications [73]. There were only 6 minor adverse events which included transient dizziness (n=3), transient arm weakness (n=2), and facial flushing (n=1) [73].

Codman's Manipulation technique

Codman's manipulation includes three consecutive 90° rotations called elevation, swing, and descending movements.

(1) Starting position: The patient hangs his or her arm along the side with the thumb pointing forward and fingers pointing toward the ground.

(2) Elevation (first move): The arm is elevated 90° in the sagittal plane without rotation about the humeral shaft axis (i.e., thumb points upward and fingers point forward).

(3) Swing (second move): The arm is moved 90° to the coronal plane without rotation about the humeral shaft axis (i.e., fingers now point to the right or left for the right and left shoulders, respectively).

(4) Descending (third move): Finally, the arm is lowered 90° downward (i.e., fingers point to the ground). After these three rotations, the patient will notice that the thumb points to the right or left (for the right and left shoulders, respectively), which means that the arm has rotated by 90° [16,17].

A general law of motion was proposed to answer the question of Codman's paradox, which is stated as when the long-axis of the arm performs a closed-loop motion by three sequential rotations known as Codman's rotations, it produces an equivalent axial rotation angle about the long-axis. The equivalent axial rotation angle equals the angle of swing. Validity of the proposed law of motion is demonstrated by computer simulation of various Codman's rotations [17].

Combined approach of SSNB followed by Codman's manipulation and home exercises

We studied a combined approach including SSNB followed by Codman's manipulation of the glenohumeral joint and a home program of ROM exercises, pendulum exercises for the arm and stretching techniques for the shoulder joint in patients with idiopathic frozen shoulder [74]. We found active range of motion increased significantly for flexion, abduction, internal rotation and external rotation. A significant decrease of visual analog scale and shoulder disability Questionnaire scores between baseline and follow-up assessments at 1, 6 and 12 weeks post manipulation was also observed [74]. Extension of pain relief for 12 weeks post injection is beyond the pharmacological effect of the drug. There are many possible explanations, including a decrease in central sensitization of dorsal horn nociceptive neurons. In addition, depletion of substance P and nerve growth factor in the synovium and afferent C fibers of the glenohumeral joint after the blockade may also contribute to the long-term relief. Furthermore, a 'wind down' (a reduction in peripheral nociceptive input) has been suggested [56,75,76]

In this combined approach, instead of manipulating the shoulder under general anaesthesia in the operating room, Codman's manipulation following SSNB was used in the outpatient clinic, thus reducing the risk of general anaesthesia, patient discomfort, and treatment cost. Furthermore, no complications were encountered and patients tolerated the procedure well.

Our results were comparable to those of Hollis et al. [77] who performed Codman's manipulation under general anaesthesia in patients with frozen shoulder in terms of reduction of pain and disability and improvement of ROM. In a previous study, Khan et al. [78] performed manipulation for the glenohumeral joint following SSNB and intra-articular local anaesthesia in patients with idiopathic frozen shoulder, showing a significant decrease in VAS and increase in ROM; however, shoulder disability was not assessed. Our results were similar to those of Khan and colleagues, although we used a different type of manipulation, no intra- articular anaesthesia was used and shoulder disability was assessed using the Shoulder Disability Questionnaire. An additional study was performed by Mitra et al. [79] on patients with frozen shoulder in whom SSNB was performed followed by intra-articular shoulder injection with steroid and local anaesthetic, and finally manipulation was performed in flexion and abduction movements only. The results of our study are in accordance with those of Mitra and colleagues, although our patients were not subjected to the risk of intra-articular injection and the manipulation technique used in our study included rotational movements, thus improving ROM in internal and external rotations, in addition to flexion and abduction, in contrast to the study by Mitra and colleagues in which only flexion and abduction movements showed improvement. Ozkan et al. [80] reported an improvement in shoulder pain following SSNB. Their study varied from ours, as they included only 10 patients with frozen shoulder secondary to diabetes mellitus, which was excluded from our study; no manipulations were performed and shoulder disability was not assessed. Yet, the results of Ozkan and

colleagues support our results in the efficacy of SSNB and provide a hope for the management of pain in frozen shoulder.

In a recent meta-analysis of randomized trials, eleven randomized controlled trials that compared SSNB with physical therapy, placebo, and intra-articular injections were included, comprising 591 patients. Regarding pain relief, SSNB provided better pain relief for 12 weeks compared with physical therapy and placebo injections, but was not superior to intra-articular injections. Differences in patient populations and use of pulsed radiofrequency did not cause a significant variation in therapeutic efficacy, but guidance using ultrasound showed consistently better effectiveness than guidance using surface landmarks and fluoroscopy [81].

Conclusion

Combined approach of SSNB followed by Codman's manipulation and home exercises proved to accelerate the recovery of idiopathic frozen shoulder. This combined approach is effective and safe to be administered in outpatient clinics by a well-trained physician, offering clear advantages (ease of application, low cost, rare side effects) and considering that the top priority of a pain control program is restoration of function to perform usual ADL. It may prove to be a useful treatment for patients who are unfit or unwilling to consider manipulation under anaesthesia. Further, there are economic benefits as patients are able to return to work sooner without the need for hospitalization or spending time in physical therapy sessions.

Compliance with ethical standards

Conflict of interest

There are no competing interests (financial/potential influence of the contents/ other relationships or activities) involved in this work.

References

1. Codman EA (1934) Rupture of the supraspinatus tendon and other lesions in or about the subacromial bursa. The shoulder, RE Kreiger.
2. Neviaser J (1945) Adhesive capsulitis of the shoulder: a study of the pathological findings in periarthritis of the shoulder. J Bone Joint Surg 27: 211-222.
3. Laubscher P, Rösch TG (2009) Frozen shoulder: a review. SA Orthopedic Journal Spring: 24-29.
4. Dias R, Cutts S, Massoud S (2005) Frozen shoulder. BMJ 331: 1453-1456.
5. Fernandes MR (2014) Arthroscopic treatment of refractory adhesive capsulitis of the shoulder. Rev Col Bras Cir 41: 30-35.
6. Favejee MM, Huisstede BM, Koes BW (2011) Frozen shoulder: the effectiveness of conservative and surgical interventions – systematic review. Br J Sports Med 45: 49-56.
7. Lorbach O, Anagnostakos K, Scherf C, Seil R, Kohn D, et al. (2010) Nonoperative management of adhesive capsulitis of the shoulder: oral cortisone application versus intra-articular cortisone injections. J Shoulder Elbow Surg 19: 172-179.
8. Borglum J, Bartholdy A, Hautopp H, Krogsgaard MR, Jensen K (2011) Ultrasound-guided continuous suprascapular nerve block for adhesive capsulitis: one case and a short topical review. Acta Anaesthesiol Scand 55: 242-247.
9. Iqbal MJ, Anwar W, Rahman N, Kashif S, Khan A (2012) Suprascapular nerve block in the treatment of frozen shoulder. J Surg Pak 17: 27-31.
10. Yasar E, Vural D, Safaz I, Balaban B, Yilmaz B, et al. (2011) Which treatment approach is better for hemiplegic shoulder pain in stroke patients: intra-articular steroid or suprascapular nerve block? A randomized controlled trial. Clin Rehabil 25: 60-68.
11. Dahan TH, Fortin L, Pelletier M, Petit M, Vadeboncoeur R, et al. (2000) Double blind randomized clinical trial examining the efficacy of bupivacaine suprascapular nerve blocks in frozen shoulder. J Rheumatol 27: 1464-1469.
12. Di Lorenzo L, Pappagallo M, Gimigliano R, Palmieri E, Saviano E, et al. (2006) Pain relief in early rehabilitation of rotator cuff tendinitis: any role for indirect suprascapular nerve block? Eura Medicophys 42: 195-204.
13. Amir-Us-Saqlain H, Zubairi A, Taufiq I (2007) Functional outcome of frozen shoulder after manipulation under anaesthesia. J Pak Med Assoc 57: 181-185.
14. Reeves B (1975) The natural history of the frozen shoulder syndrome. Scand J Rheumatol 4: 193-196.
15. Hamdan TA, Al-Essa KA (2003) Manipulation under anaesthesia for the treatment of frozen shoulder. Int Orthop 27: 107-109.
16. Codman EA (1934) The shoulder. Boston. Mass: Thomas Todd 216-224.
17. Cheng PL (2006) Simulation of Codman's paradox reveals a general law of motion. J Biomech 39: 1201-1207.
18. Hannafin JA, Chiaia TA (2000) Adhesive capsulitis. A treatment approach. Clin Orthop Relat Res 372: 95-109.
19. Castellarin G, Ricci M, Vedovi E, Vecchini E, Sembenini P, et al. (2004) Manipulation and arthroscopy under general anesthesia and early rehabilitative treatment for frozen shoulders. Arch Phys Med Rehabil 85: 1236-1240.
20. Arslan S, Celiker R (2001) Comparison of the efficacy of local corticosteroid injection and physical therapy for the treatment of adhesive capsulitis. Rheumatol Int 21: 20-23.
21. Hakim AJ, Cherkas LF, Spector TD, MacGregor AJ (2003) Genetic associations between frozen shoulder and tennis elbow: a female twin study. Rheumatology (Oxford) 42: 739-742.
22. Grey RG (1978) The natural history of "idiopathic" frozen shoulder. J Bone Joint Surg Am 60: 564.
23. DePalma AF (2008) The classic. Loss of scapulohumeral motion (frozen shoulder). Clin Orthop Relat Res 466: 552-560.
24. Murnaghan JP (1990) Frozen shoulders in the Shoulder. Edited by Charles A. Rockwood JR, and Matsen FA, III. Philadelphia, W. B. Saunders 837-862.
25. Hand GCR, Athanasou NA, Carr AJ (2005) The pathology of frozen shoulder: a chronic inflammation mast cell mediated proliferative fibrosis.
26. Rodeo SA, Hannafin JA, Tom J, Warren RF, Wickiewicz TL (1997) Immunolocalization of cytokines and their receptors in adhesive capsulitis of the shoulder. J Orthop Res 15: 427-436.
27. McGinty JB, Burkhart SS, Johnson DH, Jackson RW, Richmond JC (2002) Operative arthroscopy. (3rd edn), Lippincott Williams and Wilkins, 558-569.
28. Harryman DT, Lazurus MD, Rozencwaig R (2004) The stiff shoulder. In: Rockwood CA, Matsen FA, Wirth MA, Lippitt SB, editors. The shoulder. (3rd edn), Philadelphia: Saunders.
29. Lundberg J (1969) The frozen shoulder. Clinical and radiographical observations. The effect of manipulation under general anaesthesia. Structure and glycosaminoglycan content of the joint capsule. Local bone metabolism. Acta Orthop Scand 119: 1-59.
30. Rizk TE, Pinals RS, Talaiver AS (1991) Corticosteroid injections in adhesive capsulitis: investigation of their value and site. Arch Phys Med Rehabil 72: 20-22.
31. Ozaki J, Nakagawa Y, Sakurai G, Tamai S (1989) Recalcitrant chronic adhesive capsulitis of the shoulder. Role of contracture of the coracohumeral ligament and rotator interval in pathogenesis and treatment. J Bone Joint Surg Am 71: 1511-1515.

32. Binder AI, Bulgen DY, Hazleman BL, Roberts S (1984) Frozen shoulder: a long-term prospective study. Ann Rheum Dis. 43: 361–364.
33. Thierry D (2005) Adhesive capsulitis. E medicine 11: 7.
34. Binder AI, Bulgen DY, Hazleman BL, Tudor J, Wraight P (1984) Frozen shoulder: an arthrographic and radionuclear scan assessment. Ann Rheum Dis 43: 365-369.
35. Sheridan MA, Hannafin JA (2006) Upper extremity: emphasis on frozen shoulder. Orthop Clin North Am 37: 531-539.
36. Buchbinder R, Hoving JL, Green S, Hall S, Forbes A, et al. (2004) Short course prednisolone for adhesive capsulitis (frozen shoulder or stiff painful shoulder): a randomised, double blind, placebo controlled trial. Ann Rheum Dis 63: 1460-1469.
37. Ryans I, Montgomery A, Galway R, Kernohan WG, McKane R (2005) A randomized controlled trial of intra-articular triamcinolone and/or physiotherapy in shoulder capsulitis. Rheumatology (Oxford) 44: 529-535.
38. Buchbinder R, Green S, Youd JM (2003) Corticosteroid injections for shoulder pain. Cochrane Database Syst Rev : CD004016.
39. Carette S, Moffet H, Tardif J, Bessette L, Morin F, et al. (2003) Intraarticular corticosteroids, supervised physiotherapy, or a combination of the two in the treatment of adhesive capsulitis of the shoulder: A placebo-controlled trial. Arthritis & rheumatism 48: 829-838.
40. Jacobs LG, Smith MG, Khan SA, Smith K, Joshi M (2009) Manipulation or intra-articular steroids in the management of adhesive capsulitis of the shoulder? A prospective randomized trial. J Shoulder Elbow Surg 18: 348-353.
41. Diercks RL, Stevens M (2004) Gentle thawing of the frozen shoulder: a prospective study of supervised neglect versus intensive physical therapy in seventy-seven patients with frozen shoulder syndrome followed up for two years. Journal of Shoulder and Elbow Surgery 13: 499-502.
42. Ginn K, Cohen M (2005) Exercise therapy for shoulder pain aimed at restoring neuromuscular control: a randomized comparative clinical trial. Journal of Rehabilitation Medicine 37: 115-122.
43. Andren L, Lundberg BJ (1965) Treatment of Rigid Shoulders by Joint Distension During Arthrography. Acta Orthop Scand 36: 45-53.
44. Gavant ML, Rizk TE, Gold RE, Flick PA (1994) Distention arthrography in the treatment of adhesive capsulitis of the shoulder. J Vasc Interv Radiol 5: 305-308.
45. Fouquet B, Griffoul I, Borie MJ, Roger R, Bonnin B, et al. (2006) Adhesive capsulitis: evaluation of a treatment coupling capsular distension and intensive rehabilitation. In Annales de réadaptation et de médecine physique: revue scientifique de la Société française de rééducation fonctionnelle de réadaptation et de médecine physique 49: 68-74.
46. Quraishi NA, Johnston P, Bayer J, Crowe M, Chakrabarti AJ (2007) Thawing the frozen shoulder: A Randomised Trial Comparing Manipulation Under Anaesthesia With Hydrodilatation. Journal of Bone & Joint Surgery 89: 1197-1200.
47. Duplay S (1872) De la peri-arthrite scapulo-humerale et des raideurs de l'epaule qui en sont la consequence. Arch Gen Med 20: 513-542.
48. Reeves B (1966) Arthrographic changes in frozen and post-traumatic stiff shoulders. Proc R Soc Med 59: 827-830.
49. Andersen NH, Søjbjerg JO, Johannsen HV, Sneppen O (1998) Frozen shoulder: arthroscopy and manipulation under general anesthesia and early passive motion. J Shoulder Elbow Surg 7: 218-222.
50. Holloway GB, Schenk T, Williams GR, Ramsey ML, Iannotti JP (2001) Arthroscopic capsular release for the treatment of refractory postoperative or post-fracture shoulder stiffness. J Bone Joint Surg Am 83-83A: 1682-7.
51. Waldburger M, Meier JL, Gobelet C (1992) The frozen shoulder: diagnosis and treatment. Prospective study of 50 cases of adhesive capsulitis. Clin Rheumatol 11: 364-368.
52. Levine WN, Kashyap CP, Bak SF, Ahmad CS, Blaine TA, et al. (2007) Nonoperative management of idiopathic adhesive capsulitis. J Shoulder Elbow Surg 16: 569-573.
53. Eljabu W, Klinger HM, von Knoch M (2016) Prognostic factors and therapeutic options for treatment of frozen shoulder: a systematic review. Archives of orthopaedic and trauma surgery 136: 1-7.
54. Aszmann OC, Dellon AL, Birely BT, McFarland EG (1996) Innervation of the human shoulder joint and its implications for surgery. Clin Orthop Relat Res : 202-207.
55. Ritchie ED, Tong D, Chung F, Norris AM, Miniaci A, et al. (1997) Suprascapular nerve block for postoperative pain relief in arthroscopic shoulder surgery: a new modality? Anesth Analg 84: 1306-1312.
56. Chan CW, Peng PW (2011) Suprascapular nerve block: a narrative review. Reg Anesth Pain Med 36: 358-373.
57. Wertheim HM, Rovenstein EA (1941) Suprascapular nerve block. Anesthesiology 2: 541-545.
58. Moore DC (1979) Block of the suprascapular nerve. In: Moore DC, editor. Regional block (4th edn), Springfield: Charles C Thomas Co.
59. Gordh T (1979) Suprascapular nerve block. In: Eriksson E, editor. Illustrated handbook in local anaesthesia. (2nd edn), Copenhagen: Munksgaard.
60. Katz J (1951) Atlas of regional anaesthesia. 2nd edn. Norwalk: Appleton; 1994.
61. Granirer LW (1951) A simple technic for suprascapular nerve block. N Y State J Med 51: 1048.
62. Breen TW, Haigh JD (1990) Continuous suprascapular nerve block for analgesia of scapular fracture. Can J Anaesth 37: 786-788.
63. Dangoisse MJ, Wilson DJ, Glynn CJ (1994) MRI and clinical study of an easy and safe technique of suprascapular nerve blockade. Acta Anaesthesiol Belg 45: 49-54.
64. Barber FA (2005) Suprascapular nerve block for shoulder arthroscopy. Arthroscopy 21: 1015.
65. Feigl GC, Anderhuber F, Dorn C, Pipam W, Rosmarin W, et al. (2007) Modified lateral block of the suprascapular nerve: a safe approach and how much to inject? A morphological study. Reg Anesth Pain Med 32: 488-494.
66. Shanahan EM, Ahern M, Smith M, Wetherall M, Bresnihan B, et al. (2003) Suprascapular nerve block (using bupivacaine and methylprednisolone acetate) in chronic shoulder pain. Ann Rheum Dis 62: 400-406.
67. Gorthi V, Moon YL, Kang JH (2010) The effectiveness of ultrasonography-guided suprascapular nerve block for perishoulder pain. Orthopedics 33.
68. Jeon WH, Park GW, Jeong HJ, Sim YJ (2014) The comparison of effects of suprascapular nerve block, intra-articular steroid injection, and a combination therapy on hemiplegic shoulder pain: pilot study. Ann Rehabil Med 38: 167-173.
69. Adey-Wakeling Z, Crotty M, Shanahan EM (2013) Suprascapular nerve block for shoulder pain in the first year after stroke: a randomized controlled trial. Stroke 44: 3136-3141.
70. Taskaynatan MA, Yilmaz B, Ozgul A, Yazicioglu K, Kalyon TA (2005) Suprascapular nerve block versus steroid injection for non-specific shoulder pain. Tohoku J Exp Med 205: 19-25.
71. Shrestha BR, Maharjan SK, Shrestha S, Gautam B, Thapa C, et al. (2007) Comparative study between tramadol and dexamethasone as an admixture to bupivacaine in supraclavicular brachial plexus block. JNMA J Nepal Med Assoc 46: 158-164.
72. Colombo G, Padera R, Langer R, Kohane DS (2005) Prolonged duration local anaesthesia with lipid–protein–sugar particles containing bupivacaine and dexamethasone. J Biomed Mater Res A 75: 458-464.
73. Shanahan EM, Shanahan KR, Hill CL, Ahern MJ, Smith MD (2012) Safety and acceptability of suprascapular nerve block in rheumatology patients. Clin Rheumatol 31: 145-149.
74. El-Badawy MA, Fathalla MM (2014) Suprascapular nerve block followed by Codman's manipulation and exercise in the rehabilitation of idiopathic frozen shoulder. Egyptian Rheumatology and Rehabilitation 41: 172.

75. Birklein F, Schmelz M (2008) Neuropeptides, neurogenic inflammation and complex regional pain syndrome (CRPS). Neurosci Lett 437: 199-202.

76. Schaible HG (2007) Peripheral and central mechanisms of pain generation. Handb Exp Pharmacol 177: 3-28.

77. Hollis R, Lahav A, West HS Jr (2006) Manipulation of the shoulder using Codman's paradox. Orthopedics 29: 971-973.

78. Khan JA, Devkota P, Acharya BM, Pradhan NM, Shreshtha SK, et al. (2009) Manipulation under local anesthesia in idiopathic frozen shoulder--a new effective and simple technique. Nepal Med Coll J 11: 247-253.

79. Mitra R, Harris A, Umphrey C, Smuck M, Fredericson M (2009) Adhesive capsulitis: a new management protocol to improve passive range of motion. PM R 1: 1064-1068.

80. Ozkan K, Ozcekic AN, Sarar S, Cift H, Ozkan FU, et al. (2012) Suprascapular nerve block for the treatment of frozen shoulder. Saudi J Anaesth 6: 52-55.

81. Chang KV, Hung CY, Wu WT, Han DS, Yang RS, et al. (2015) Comparison of the Effectiveness of Suprascapular Nerve Block with Physical Therapy, Placebo, and Intra-articular Injection in Management of Chronic Shoulder Pain-a Meta-analysis of Randomized Controlled Trials. Archives of physical medicine and rehabilitation 15: 01476-01478.

Analgesic Effect of Extracorporeal Shock Wave Treatment Combined with Fascial Manipulation Theory for Adhesive Capsulitis of the Shoulder: A Retrospective Study

Objectives. This study aims to explore whether extracorporeal shockwave treatment (ESWT) based on the theory of fascial manipulation (FM) at select treatment points is superior to traditional local ESWT for pain relief in adhesive capsulitis of the shoulder. *Methods*. Data from patients with adhesive capsulitis of the shoulder who received weekly ESWT according to fascial manipulation theory (ESWT-FM) or local extracorporeal shockwave treatment (L-ESWT) during a 5-week treatment period were evaluated. Pain-on-movement numeric rating scale (p-NRS) and range of motion (ROM) testing were performed before the treatment period, after the first treatment, and after the fifth treatment. *Results*. There were significant reductions in pain scores in the ESWT-FM group ($p < 0.05$) after the first treatment, and after the fifth treatment, both groups had marked, significant improvement ($p < 0.05$), with a significantly greater reduction in pain (p-NRS) in the ESWT-FM group compared to the L-ESWT group ($p < 0.05$). There was no significant difference in terms of ROM in the L-ESWT group, while there was slight improvement of forward flexion in the ESWT-FM group after the fifth treatment. *Conclusions*. ESWT-FM provided faster pain relief and slightly more notable improvement of function compared with L-ESWT for the patients with adhesive capsulitis of shoulder.

1. Introduction

Shoulder pain is a common musculoskeletal malady, and one of the most prevalent causes of shoulder pain is adhesive capsulitis of the shoulder (AC), which may be associated with minor trauma, environmental stresses, autoimmune processes, or disease like diabetes mellitus and so forth [1, 2]. AC results from inflammation, fibrosis, and contracture of the joint capsule or adjacent bursa, which manifests as a progressive loss of active and passive shoulder movement accompanied by pain [1, 3]. In a retrospective review of 234 patients, 89.5% of AC cases were treated successfully without the need for surgical intervention [4]. Nonsurgical or minimally invasive treatment options for AC include nonsteroidal anti-inflammatory medications, corticosteroid injection at the affected area, hydrodilatation, manipulation under anaesthesia, and physiotherapy [3, 5]. More recently, extracorporeal shockwave therapy (ESWT), as a sort of physical factor, has been proven to be effective for relief of painful shoulder conditions, including AC [6, 7] and supraspinatus tendinopathy [8]. Most of the current literature on ESWT for musculoskeletal disorders has focused on its use in the treatment of bone disorders, including osteonecrosis of femoral head and nonunion of bones [9, 10], and treatment of tendinopathies [10, 11], including lateral elbow epicondylitis [12], plantar fasciopathy [13], calcific tendinitis of shoulder [14], and patellar tendinopathy [15]. Previous ESWT studies have typically focused on application to painful and local treatment points localized in the affected tendon, muscle, or bone [6–8, 10, 11]. And in prior evaluations of ESWT for AC, although the number of studies is very small, the treatment was usually applied only to local tender points also with inconclusive results [6, 7].

During recent years, the critical role of the fascia in the pathogenesis of musculoskeletal pain and dysfunction has gradually been accepted [16], and there is a prevailing

view that the myofascial system is a three-dimensional continuum wherein musculoskeletal disorders may be caused by changes in the deep muscle fascia, such as lack of sliding, stretching, and appropriate adaptation. Constant nonphysiological tension in a fascial segment may lead to the formation of adaptive fibroses, which may cause pain both distally and proximally [17]. In keeping with this theory, musculoskeletal dysfunction, including painful shoulder syndrome [16] and TMJ disorders [17], has been treated successfully with the novel treatment strategy of fascial manipulation (FM) at points away from the painful area [18, 19]. Under this theory of FM, determination of the appropriate treatment area for the pain of AC requires consideration of not only the local point of pain but also the related functional muscle and fascia in the surrounding region [18].

The purpose of the present study is to determine, by retrospective review, whether AC-related pain could be more effectively treated by ESWT according to FM theory than by conventional local ESWT alone.

2. Materials and Methods

The study included 34 patients who were treated for AC at Shengjing Hospital during the period between January 2015 and July 2017. Patients were included in the study if they were 18 years old or older, exhibited shoulder pain with restriction in ROM of >50% in abduction or flexion and external or internal rotation, experienced symptoms for more than 3 months or had not received treatment, had undergone shoulder radiography, soft tissue sonography, and/or shoulder magnetic resonance imaging a minimum of 14 days prior to selection for ESWT treatment, and did not receive additional pain management procedures, such as intra-articular injection or oral medication, during the therapy. Written informed consent was obtained from every patient before beginning treatments.

Patients were excluded from the study if they were pregnant, if they had had surgical intervention on the affected shoulder, if there was extensive scar around the shoulder, rotator cuff calcification, joint infection, lack of stability, rheumatoid arthritis or full thickness tear of shoulder rotator cuff, cervical radiculopathy or damage to the spinal cord, or history of cortisone injection in the affected area in the previous 6 weeks, or if they had other contraindications to shock wave treatment, including artificial pacemaker, use of anti-blood clotting medications, known bleeding disorder, known malignancy in the area intended for treatment, or epilepsy.

The patients were divided into two groups. All patients underwent 5 sessions of ESWT during each seven-day interval. One group received ESWT according to the fascial manipulation theory (ESWT-FM) and the other had local ESWT (L-ESWT) only. A Swiss DolorClast radial shockwave device (EMS Electro Medical Systems, Nyon, Switzerland) with pressure in the range of 1.5 to 2.5 bars was employed at 0.08 to 0.28 mJ/mm^2 and 10 to 13 Hz frequency. In the case of the L-ESWT group, the two chosen local tender treatment points were the anterior shoulder joint, with the superior edge of the painful treatment area being just lateral to the coracoid process, and an area that was 1 cm proximal to the tendon attachment to bone. For those in the ESWT-FM group, FM guidelines were followed to choose centers of coordination points based on the physical examination, in addition to the two local tender treatment points [15]. The horizontal plane was often chosen, and the treatment points were at the lower section of the intrarotator muscle insertions at the humerus (IR-Hu); below the elbow crease at pronator teres, for the point with highest sensitivity (IR-CU); at trapezius, immediately above the superior angle of the scapula (ER-SC); and at the posterior aspect of the rotator cuff (ER-HU), laterally to triceps tendon, in the fascia and lateral septum (ER-CU) [16]. Approximately 450 to 500 shocks were applied at every treatment point, according to the patient's tolerance. During the 5-week treatment period, local electrotherapy was administered to all patients as the standard and baseline treatment, consisting of ultra-short-wave therapy, intermediate frequency electrotherapy, or ultrasonic therapy.

Pain scores and basic shoulder functionality were assessed prior to treatment and after the first and fifth treatment sessions, based on the pain-on-movement numeric rating scale (p-NRS), with a range of 0 (no pain) to 10 (severe pain), and range of motion (ROM) testing, which evaluated forward flexion, abduction, and internal and external rotation.

2.1. Statistical Analysis. The Statistical Package for the Social Sciences v16.0 (SPSS Inc., Chicago, Illinois) was used for data collection and analysis. Independent samples t-test and repeated-measures one-way analysis of variance (ANOVA) were, respectively, used for intergroup and intragroup analyses. Statistical significance was indicated by two-sided p values of <0.05.

3. Results

There were 16 patients in the ESWT-FM group and 18 patients in the L-ESWT group. The groups did not differ significantly at baseline in terms of affected side, duration of pain, and p-NRS (Table 1).

After the first treatment, p-NRS showed a statistically significant improvement in both groups ($p < 0.05$), and there was significantly more improvement in the ESWT-FM group compared to the L-ESWT group ($p = 0.0001$) (Figure 1). After the fifth treatment, both groups showed remarkable improvement ($p < 0.05$), and again the improvement in p-NRS was significantly greater in the ESWT-FM group compared to the L-ESWT group ($p = 0.0001$) (Figure 1).

We only observed slight significant improvement in forward flexion in the ESWT-FM group after the fifth treatment ($p = 0.001$), and there was a significant difference between groups ($p = 0.001$). There was no significant difference in terms of range of motion in either group other than the improvement in forward flexion in the ESWT-FM group after the first and fifth treatment sessions, and there was no significant difference between groups (Table 2).

Table 1: Baseline clinical characteristics.

	Number (female/male)	Age (year)	Duration of pain (month)	Affected side (left/right)	p-NRS
ESWT-FM group	16 (9/7)	53.6 ± 5.1	4.1 ± 0.6	5/11	6.7 ± 0.8
L-ESWT group	18 (10/8)	52.8 ± 4.9	3.9 ± 0.4	6/12	6.4 ± 0.9

ESWT-FM: extracorporeal shockwave therapy combined with fascial manipulation theory; L-ESWT: local extracorporeal shockwave treatment.

Table 2: Comparison of range of motion results after ESWT-FM and L-ESWT.

	Baseline	After 1st treatment	After 5th treatment
ESWT-FM group			
Forward flexion	75.1 ± 12.5	81.8 ± 10.3	90.1 ± 9.3*#
Lateral abduction	57.9 ± 13.3	62.3 ± 14.5	66.7 ± 15.9
External rotation	10.5 ± 4.1	11.6 ± 4.9	12.4 ± 4.9
Internal rotation	14.8 ± 6.6	16.1 ± 7.4	17.1 ± 8.1
L-ESWT group			
Forward flexion	73.7 ± 11.2	75.3 ± 11.9	77.1 ± 11.8
Lateral abduction	56.8 ± 14.7	58.7 ± 14.9	61.5 ± 14.9
External rotation	9.9 ± 4.3	10.5 ± 4.4	11.7 ± 4.6
Internal rotation	15.2 ± 7.1	15.9 ± 7.3	16.9 ± 7.6

ESWT-FM: extracorporeal shockwave therapy combined with fascial manipulation theory; L-ESWT: local extracorporeal shockwave treatment; *range of motion after treatment versus baseline, $p < 0.05$. #Range of motion after treatment; comparison between groups, $p < 0.05$.

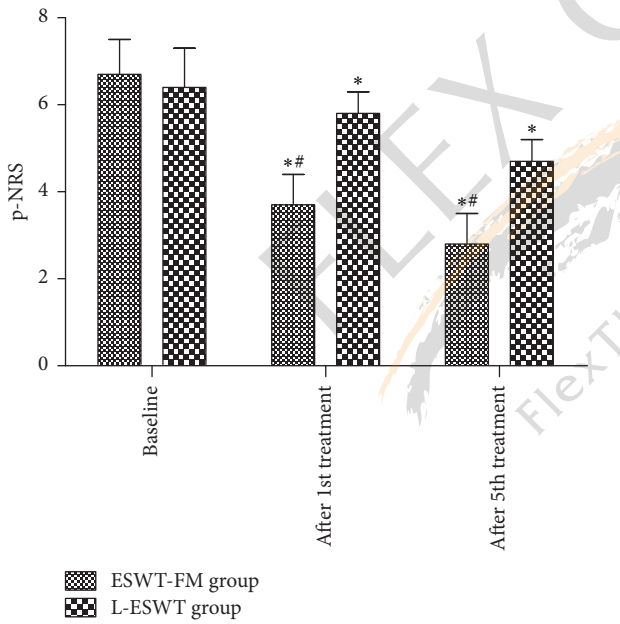

Figure 1: Comparison of p-NRS after ESWT-FM and L-ESWT. ESWT-FM: extracorporeal shockwave therapy combined with fascial manipulation theory; L-ESWT: local extracorporeal shockwave treatment. ∗ indicates comparison of p-NRS after treatment versus baseline, $p < 0.05$; #p-NRS after treatment; comparison between groups, $p < 0.05$.

4. Discussion

We found that both treatment groups experienced pain relief but that the relief was quicker and was more significant after ESWT-FM, both after the first treatment session and after the overall treatment. This finding corroborated the results of earlier studies. When ESWT treatment was compared with oral steroids for treatment of AC, improvements in the total constant shoulder score and in the activities of daily living and ROM parameters of that score were statistically significant in the ESWT group from study commencement to the sixth week, while the pain and power parameters were statistically significant between the second and fourth weeks [6]. While some studies note better results with ESWT [7], others have found only limited efficacy for the treatment of shoulder pain [8, 20]. In the present study, ESWT-FM was associated with a 50% reduction in p-NRS after a single session, suggesting quicker pain relief.

The treatment points chosen in this study were not the same as those in earlier studies. In addition to conventional points around the shoulder (e.g., affected rotator interval and coracohumeral ligament) [1], several centers of coordination points were chosen as well, based on the physical examination and in accordance with the FM guidelines. FM theory construes the myofascial system as a three-dimensional continuum, and musculoskeletal dysfunction occurs when there is lack of sliding, stretching, and appropriate adaptation of the muscular fascia. The shoulder is viewed as part of this interconnected system, and its functionality depends on how it interacts with the other components of the system [17–19]. Issues arising in the shoulder can lead to alterations in the local fascia, which in turn will cause further changes or referred pain in distal or proximal segments (e.g., elbow or wrist joint), while the constant nonphysiological tension in the deep fascia of the affected area can induce the formation of adaptive fibrosis [16]. Therefore, to minimize the likelihood of fibrosis, restore physiological tension in the deep fascia, and facilitate rapid alleviation of pain, distal points over the

deep fascia are chosen as treatment points, as they were in this study.

We observed a slight improvement in forward ROM after FM-ESWT. It is known that both pain relief and ROM improvements are possible with therapeutic exercises and mobilization [1, 5], and in the present study we could not distinguish which effects, ESWT-FM or the standard exercise program, contributed most to the ROM improvements. Certainly, pain relief and restored physiological tension in the deep fascia after ESWT-FM may have helped to improve participation in the exercise program. Nonetheless, to determine whether AC recovery is enhanced by a supervised exercise program on its own or combined with ESWT-FM, additional research must be conducted.

Due to its retrospective design, this study could not produce the same high-caliber evidence as a double-blind randomized clinical trial and, moreover, the sample was insufficiently large. Thus, to gain more data regarding the efficiency of ESWT-FM alongside therapeutic exercises and mobilization to achieve long-term pain and ROM improvements in patients with AC, additional prospective randomized blinded controlled clinical trials must be conducted.

5. Conclusions

ESWT was applied in this study according to fascial manipulation theory to both local and distal treatment points chosen in keeping with the three-dimensional continuum view of the myofascial system. According to the obtained result, notable pain and slight functionality improvements were achieved through administration of ESWT-FM.

Conflicts of Interest

The authors declare that there are no potential conflicts of interest regarding the publication of this article.

References

[1] H. V. Le, S. J. Lee, A. Nazarian, and E. K. Rodriguez, "Adhesive capsulitis of the shoulder: review of pathophysiology and current clinical treatments," *Shoulder & Elbow*, vol. 9, no. 2, pp. 75–84, 2016.

[2] X. Yuan, Z. Zhang, and J. Li, "Pathophysiology of adhesive capsulitis of shoulder and the physiological effects of hyaluronan," *European Journal of Inflammation*, vol. 15, no. 3, pp. 239–243, 2017.

[3] A. S. Neviaser and J. A. Hannafin, "Adhesive capsulitis: a review of current treatment," *The American Journal of Sports Medicine*, vol. 38, no. 11, pp. 2346–2356, 2010.

[4] W. N. Levine, C. P. Kashyap, S. F. Bak, C. S. Ahmad, T. A. Blaine, and L. U. Bigliani, "Nonoperative management of idiopathic adhesive capsulitis," *Journal of Shoulder and Elbow Surgery*, vol. 16, no. 5, pp. 569–573, 2007.

[5] T. K. Jain and N. K. Sharma, "The effectiveness of physiotherapeutic interventions in treatment of frozen shoulder/adhesive capsulitis: A systematic review," *Journal of Back and Musculoskeletal Rehabilitation*, vol. 27, no. 3, pp. 247–273, 2014.

[6] C.-Y. Chen, C.-C. Hu, P.-W. Weng et al., "Extracorporeal shockwave therapy improves short-term functional outcomes of shoulder adhesive capsulitis," *Journal of Shoulder and Elbow Surgery*, vol. 23, no. 12, pp. 1843–1851, 2014.

[7] B. Vahdatpour, P. Taheri, A. Z. Zade, and S. Moradian, "Efficacy of extracorporeal shockwave therapy in frozen shoulder," *International Journal of Preventive Medicine*, vol. 5, no. 7, pp. 875–881, 2014.

[8] E. Kvalvaag, C. Røe, K. B. Engebretsen et al., "One year results of a randomized controlled trial on radial Extracorporeal Shock Wave Treatment, with predictors of pain, disability and return to work in patients with subacromial pain syndrome," *European Journal of Physical and Rehabilitation Medicine*, 2017.

[9] A. Berner, J. C. Reichert, M. B. Müller et al., "Treatment of long bone defects and non-unions: from research to clinical practice," *Cell and Tissue Research*, vol. 347, no. 3, pp. 501–519, 2012.

[10] F. Ioppolo, J. D. Rompe, J. P. Furia et al., "Clinical application of shock wave therapy (SWT) in musculoskeletal disorders," *European Journal of Physical and Rehabilitation Medicine*, vol. 50, no. 2, pp. 217–230, 2014.

[11] D. Moya, S. Ramón, L. Guiloff, and L. Gerdesmeyer, "Current knowledge on evidence-based shockwave treatments for shoulder pathology," *International Journal of Surgery*, vol. 24, pp. 171–178, 2015.

[12] I. Köksal, O. Güler, M. Mahiroğullari, S. Mutlu, S. Çakmak, and E. Akşahin, "Comparison of extracorporeal shock wave therapy in acute and chronic lateral epicondylitis," *Acta Orthopaedica et Traumatologica Turcica*, vol. 49, no. 5, pp. 465–470, 2015.

[13] J. D. Rompe, A. Cacchio, L. Weil et al., "Plantar fascia-specific stretching versus radial shock-wave therapy as initial treatment of plantar fasciopathy," *The Journal of Bone and Joint Surgery. American Volume*, vol. 92, no. 15, pp. 2514–2522, 2010.

[14] F. Ioppolo, M. Tattoli, L. Di Sante et al., "Clinical improvement and resorption of calcifications in calcific tendinitis of the shoulder after shock wave therapy at 6 months' follow-up: A systematic review and meta-analysis," *Archives of Physical Medicine and Rehabilitation*, vol. 94, no. 9, pp. 1699–1706, 2013.

[15] S. Mani-Babu, D. Morrissey, C. Waugh, H. Screen, and C. Barton, "The effectiveness of extracorporeal shock wave therapy in lower limb tendinopathy: a systematic review," *The American Journal of Sports Medicine*, vol. 43, no. 3, pp. 752–761, 2015.

[16] J. A. Day, C. Stecco, and A. Stecco, "Application of Fascial Manipulation© technique in chronic shoulder pain-Anatomical basis and clinical implications," *Journal of Bodywork and Movement Therapies*, vol. 13, no. 2, pp. 128–135, 2009.

[17] L. Guarda-Nardini, A. Stecco, C. Stecco, S. Masiero, and D. Manfredini, "Myofascial pain of the jaw muscles: Comparison of short-term effectiveness of botulinum toxin injections and Fascial Manipulation technique," *Cranio: Journal of Craniomandibular Practice*, vol. 30, no. 2, pp. 95–102, 2012.

[18] C. Stecco and J. A. Day, "The fascial manipulation technique and its biomechanical model: A guide to the human fascial system," *International Journal of Therapeutic Massage and Bodywork: Research, Education, and Practice*, vol. 3, no. 1, pp. 38–40, 2010.

[19] M. Branchini, F. Lopopolo, E. Andreoli, I. Loreti, A. M. Marchand, and A. Stecco, "Fascial Manipulation® for chronic

Effect of Maitland Mobilization on Radiotherapy Induced Frozen Shoulder: A Case Report

Abstract

Background: Frozen shoulder is the most prevalent case in musculoskeletal conditions due to disuse or after shoulder injury it was a different case to treat as the frozen shoulder may was induced due to radiotherapy on same hand after cancer colon.

Objective: To evaluate the effect of Maitland mobilization on radiotherapy induced frozen shoulder

Method: We reported unique case in oncology was a 50 year old female having radiotherapy induced frozen shoulder after treated with a case of colon cancer. In the present study with the other symptoms of Cancer colon treated with radiotherapy we reported the effect of frozen shoulder with in Maitland Mobilization and conventional therapy on frozen shoulder.

Outcome measure: Numerical pain rating scale, Range of Motion and Penn shoulder score

Result: There was a significant difference noted in the pain and increased in range of motion.

Conclusion: Maitland mobilization proved to be effective in radiotherapy induced frozen shoulder.

Keywords: Radiotherapy induced frozen shoulder; Maitland mobilization; penn

Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" is derived by Harold Merskey, in 1979 by IASP (International Association for the study of pain) [1]. Pain compromises the quality of life and decline in physical function leading to psychological distress and disturbed social interaction. A series of common pain syndromes in patients with cancer and cancer induced anticancer therapy have been studied (that includes pain associated with direct tumor infiltration, pain resulting from chemotherapy and radiotherapy) and pain unrelated to the cancer or cancer therapy. Survey have demonstrated that 35%-65% of cancer patients experience pain during active anticancer therapy [2] and more than two third among those with advanced diseases. Appropriate management is dependent on their careful evaluation.

Radiotherapy induced-frozen shoulder is a very rare and sensitive case to treat as it has symptoms of radiotherapy effect like pain, tiredness, and fatigue and skin sensitivity. Along with this it may have lymphoedema in axilla, weakening of the bone in the treated bone, may have damage to the nerves in the arm on the treated side that causes tingling, numbness, pain, weakness and possibly loss in movement [3]. Hence with most of the above symptoms we have to treat the frozen shoulder symptoms with the primary goal as to increase the range of motion with quality of life.

Case Report

The patient in this study was 53 years female, who gave the history of Stage III colon Cancer, treated with colectomy from October 2016 and followed by radiotherapy till May 17 and other anticancer drug therapy. Her previous medical history was not significant for diabetes mellitus and hypertension. After some sessions she developed tightness and restrictions in the arm movements that was treated with radiotherapy. Medications included at the time were Tab Pantodac 40 mg and Tab Emeset 4 mg twice a day. The patient gave a written informed consent to participate in the study and the treatment was started. Patient concern was to increase the shoulder range, reduction of pain and improve quality of life (Figures 1 and 2).

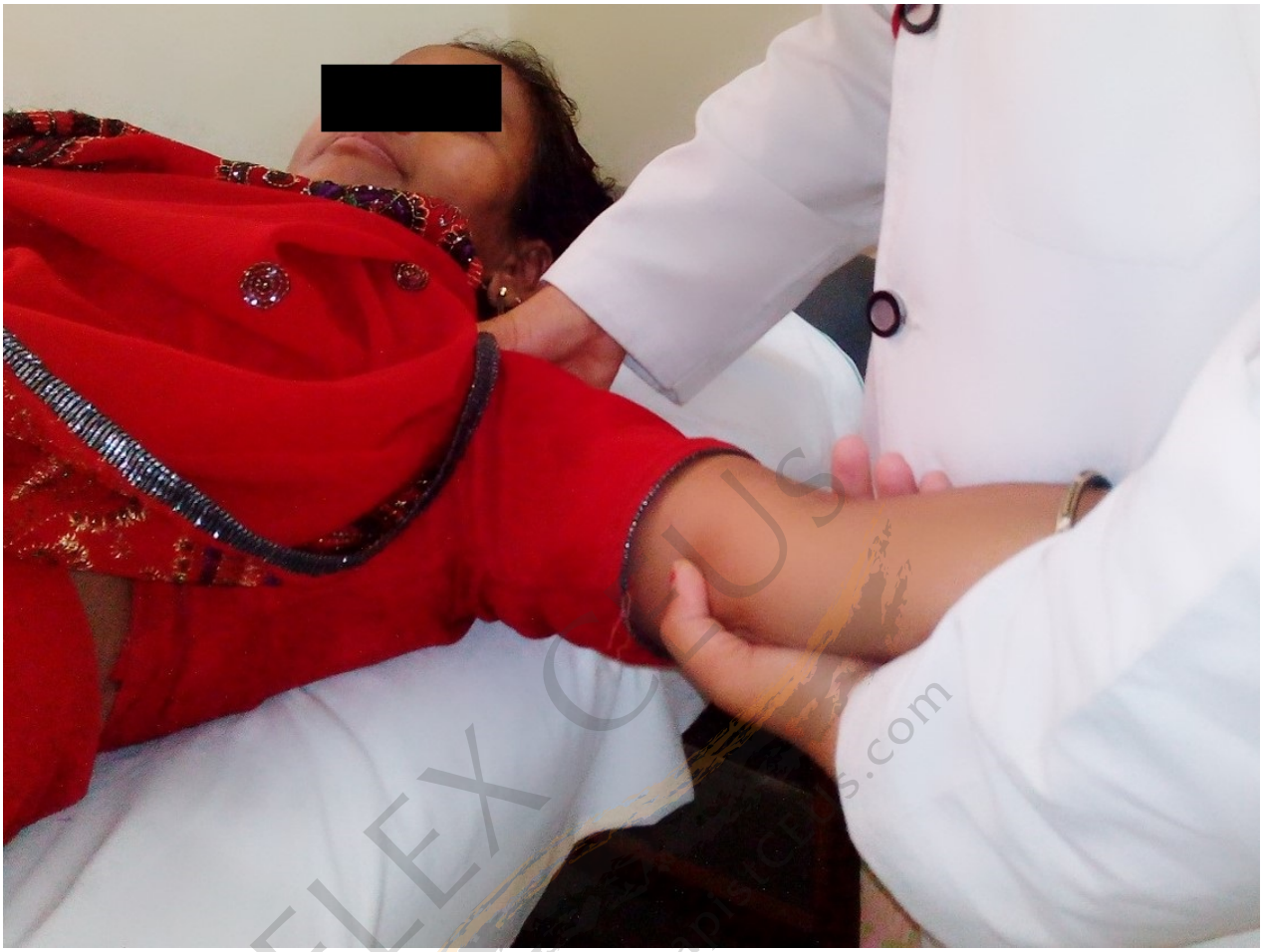

Figure 1: Examination and Assessment.

On examination and assessment subject gave a history of stiffness of the left shoulder joint since 3 months. Symptoms aggravated since last 15 days. Subject found difficulty to perform her daily activities and her pain often worsened at night and also had difficulty in sleeping on the affected side. No warmth and tenderness was noted around the shoulder joint. Capsular pattern was present. Numerical pain rating scale is valid and reliable tool to measure pain intensity [4]. The subject's pre assessment score for the left shoulder joint was 5/10 (moderate).

Shoulder	Pre intervention	Post intervention
Flexion	70˚	115˚
Extension	27˚	52˚
Abduction	50	100˚
Internal rotation	35˚	43˚
External rotation	30˚	37˚

Table 1: The pre and post interventions for shoulder are described.

The pre ranges for the shoulder joint is as described in Table 1. Penn shoulder score [5] is a 100 point scale which consists of 3 subscales including pain, satisfaction and function. The subject's pre intervention score was 40/100.

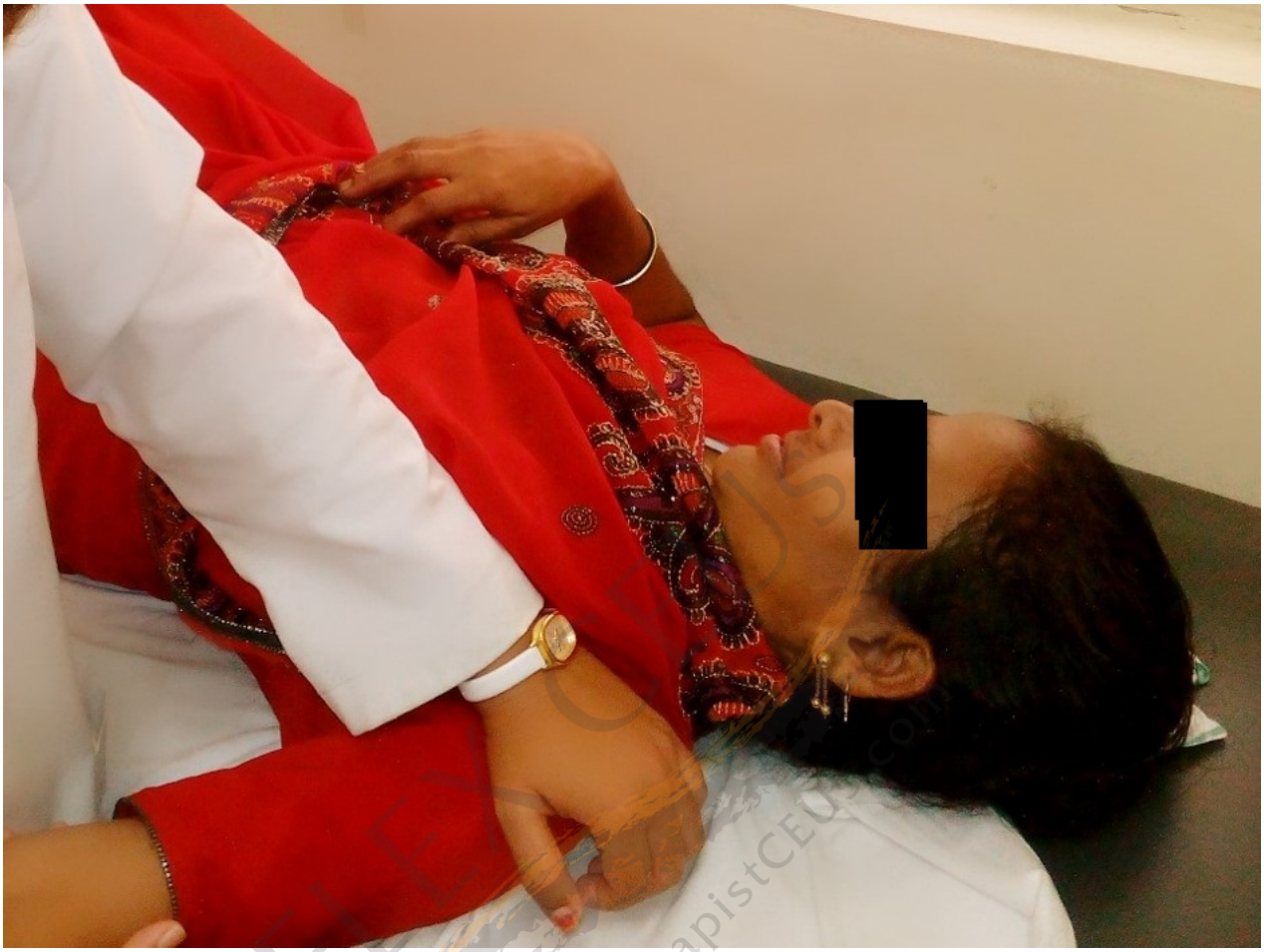

Figure 2: Shows Manual therapy.

Discussion

The subject underwent 10 consecutive sessions for 10 days. Each session lasted approximately 45 min. Initially hot moist pack was given around the left shoulder joint for 15 minutes. Manual therapy is well known to work in multitude of different mechanisms to be effective and understanding the neurological, physiological, psychophysiological mechanisms with clinically competent and safe manner [6]. We gave list necessary exercises in the present case to reduce the fatigue and tiredness that was due to radiotherapy effect. According to Harvard Medical school [7] stretching and strengthening exercises for frozen shoulder were advised to the subject which included pendulum stretch (10 revolutions in each direction, once a day), towel stretch (10-20 times a day), finger walk (10-20 times a day), cross body reach (10-20 times a day), armpit stretch (10-20 times a day) and inward and outward rotations (10-15 times, once a day) [7]. We also not used any advanced electrotherapy modalities other than TENS to be on the safer side and planned to record the effect of manual therapy i.e. Maitland mobilization therapy.

Maitland concept effect is well known on stiff joint pain and to increase various joint range of motion within short period of time. We treated the shoulder with the posterior Maitland mobilization for the first session and 10 minutes for the following sessions at starting and at the end of the every session. Previous studies have also concluded posterior Maitland mobilization to be effective in treating pain due to frozen shoulder [8]. From second session onwards after the 10 minutes of posterior mobilization we gave grade II and III Maitland mobilization in every plan for 4 to 5 minutes each.

At the end of the session we gave Transcutaneous electrical nerve stimulation (TENS) [9] was given in conventional mode for 15 minutes with a frequency of 100 Hz and pulse width 200 μs for pain relief due to mobilization if any. The subject was asked then to warm up the shoulder with hot water bag and then perform all the exercises at home at-least 3 repetition per day.

Conclusion

In the present study patient with colon cancer treated with radiotherapy on left hand developed pain and stiffness in her left shoulder joint. Patient was treated with regular conventional physiotherapy treatment like hot moist pack and hand mobility exercises. We also gave Maitland mobilization for the same and had a positive effect on pain and joint range of motion. In the first session patient had 40% different on pain score pre and post recorded on VAS scale. Patient at the end of the fifth session had positive improvement in shoulder range of motion as shown in Table 1. Patient quality of life

was also recorded on Penn sale and had significant changes with post penn score 69/100. Patient needs to continue at-least 5 more sessions and follow up to have more recovery. In the present study with the positively significant results suggests that Maitland mobilization can also be the first line of treatment that is clinically competitive and safer in patients having frozen shoulder post radiation therapy.

Ethical Clearance

Signed inform consent was taken from the study subject.

References

1. https://en.wikipedia.org/wiki/International_Association_for_the_Study_of_Pain
2. Cancer pain: Assessment and Management edited by Eduardo D. Bruera, Russell K. Portenoy.
3. https://www.breastcancercare.org.uk/information-support/facing-breast-cancer/going-through-breast-cancer-treatment/side-effects/side
4. Oldenmenger WH, Pleun J, de Klerk C, van der Rijt CC (2013) Cut points on 0-10 numeric rating scales for symptoms included in the Edmonton Symptom Assessment Scale in cancer patients: a systematic review. J Pain Symptom Manage 45: 1083-1093.
5. Leggin BG, Michener LA, Shaffer MA, Brenneman SK, Iannotti JP, et al. (2006) The Penn shoulder score: reliability and validity. J Orthop Sports Phys Ther 36: 138-151.
6. Lederman E (2005) The Science and Practice of Manual therapy. 2nd ed. Elsevier: London.
7. https://www.health.harvard.edu/shoulders/stretching-exercises-frozen-shoulder
8. https://www.physio-pedia.com/Maitland%27s_Mobilisations#cite_note-Lederman-1
9. Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, et al. (2012) Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. The Cochrane Library.