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3 **Role of low-intensity pulsed ultrasound on lumbar spondylolysis: a**
4 **systematic review**

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13
14 **Abstract**

15 **Objective:** To systematically review the role of low-intensity pulsed ultrasound on
16 lumbar spondylolysis.

17 **Method:** Literature search was conducted on PubMed, Embase, CINAHL, Web of
18 Science, PEDro and Scopus databases to identify relevant studies published between
19 2010 and 2020 by using medical subject headings and applying Booleans, such as
20 low-intensity pulsed ultrasound OR interventional ultrasound AND lumbar spine OR
21 lumbar region AND spondylolysis OR stress fracture. Unpublished studies were hand-
22 searched in the journals, abstracts of conferences were reviewed, and citation index
23 was used for searching experts in the field and then contacting them for information.

24 Studies included were the ones that had at least one of the following outcomes: bone
25 union rate, treatment period to bone union and time to return to previous activities.

26 **Results:** Of the 243 studies identified, 228(94%) were full text articles and only
27 2(0.8%) studies were critically appraised for qualitative synthesis based on bone union
28 rate, treatment period to bone union, and time to return to previous activities.

29 **Conclusion:** Low-intensity pulsed ultrasound was found to be effective for bone union
30 and a useful therapy for quick return to playing sports in patients with lumbar
31 spondylolysis.

32 **Key Words:** Lumbar region, Spondylolysis, Interventional ultrasound, Systematic
33 review.

34

35 **Introduction**

36 Low-back pain (LBP) has emerged as an expensive health problem in many
37 countries.¹ Lumbar spondylolysis, which is the defect or abnormality of the pars
38 interarticularis and a common LBP cause², mostly occurs in males bilaterally at the
39 fifth lumbar vertebra³. It has a prevalence of 5% in children age <7 years and 6% in
40 adults⁴ and is classified as developmental, dysplastic, traumatic (acute and chronic)
41 and pathologic.⁵

42 Chronic traumatic spondylolysis is associated with stress fracture or spondylolytic
43 defect of the pars interarticularis which occurs as a result of repetitive movements
44 during extension and rotation of the lumbar spine.⁶ Mostly, patients present with pain,
45 joint limitation, muscle spasm, sacral flattening and waddling gait pattern.⁷ In severe
46 cases, tightness of hamstring and iliopsoas may also occur along with posterior pelvic
47 tilt.⁸ During examination, pain is reproduced on performing the single-leg
48 hyperextension test.⁹ According to the computed tomography (CT) findings, it is
49 classified as early, progressive and terminal.¹⁰ Early-stage spondylolysis refers to the
50 stress fracture in which bone union can be achieved conservatively. However, in
51 progressive and terminal stages, spondylolytic defect occurs in which bone union is
52 delayed and cannot be obtained through conservative interventions, such as hard or
53 soft braces.¹¹ If this condition remained untreated, it can progress to
54 spondylolisthesis.¹²

55 Early diagnosis and treatment is the key to complete bone union through conservative
56 interventions, such as activity restriction and usage of thoracolumbosacral brace for 3-6
57 months.¹³ However, treatment time is very long in many cases.¹⁴ Previous studies have

58 reported that low-intensity pulsed ultrasound (LIPUS) is effective for reducing pain,
59 treatment time, and promoting bone union both in animal and human trials.¹⁵ LIPUS
60 has been used in medicine as a treatment modality. It is a form of energy transfer for
61 mechanical vibration. When it spreads in the organism, a certain dosage of ultrasound
62 can cause sonoporation effect that makes the cell membrane surface temporarily
63 disruptive, which promote extracellular molecules to enter the cell, causing changes of
64 the organism function and structure that is the biological effect of ultrasound.¹⁶
65 Collection and review of studies showing the role of LIPUS on lumbar spondylolysis
66 can be helpful for better interventions. To our knowledge, no such systematic review
67 has critically reviewed and appraised the role of LIPUS on lumbar spondylolysis. The
68 current systematic review was planned to fill the gap in literature.

69

70 **Materials Methods**

71 The systematic review followed the Preferred Reporting Items for Systematic Review
72 and Meta-Analyses (PRISMA) guidelines, and the protocol was registered with the
73 PROSPERO database in January 2021 (CRD42021227439).

74 Literature search was conducted on PubMed, Embase, CINAHL, Web of Science,
75 PEDro and Scopus databases to identify relevant studies published between 2010 and
76 2020 by using medical subject headings and applying Booleans, such as low-intensity
77 pulsed ultrasound OR interventional ultrasound AND lumbar spine OR lumbar region
78 AND spondylolysis OR stress fracture. Unpublished studies were hand-searched in the
79 journals, abstracts of conferences were reviewed, and citation index was used for
80 searching experts in the field and then contacting them for information.

81 Studies included were the ones that had at least one of the following outcomes: bone
82 union rate, treatment period to bone union and time to return to previous activities. All
83 observational studies were sought and considered eligible for the review. However, to
84 maintain scientific rigour, quantitative studies with only control group were included.
85 Inclusion criteria comprised both genders, human, symptomatic, mechanical LBP,
86 aged 0-60 years, lumbar vertebra, radiological evidence of spondylolysis, and

87 congenital spinal abnormalities. The exclusion criteria comprised neurological
88 deficits, other spinal pathologies, and degenerative spinal diseases.

89 Evaluation, critical appraisal of the retrieved studies and reporting of data was done by
90 two investigators independently using the Grading of recommendations, assessment,
91 development, and evaluations (GRADE) criteria.¹⁷ These were rated as high (4 point),
92 moderate (3 points), low (2 points) and very low (one/less). In terms of interpretations,
93 very low means the true effect is probably markedly different from the estimated
94 effect; low means the true effect might be markedly different from the estimated
95 effect; moderate means the true effect is probably close to the estimated effect; and
96 high means the authors have a lot of confidence that the true effect is similar to the
97 estimated effect.

98

99 **Results**

100 Of the 243 studies identified, 228(94%) were full text articles and only 2(0.8%)
101 studies were critically appraised for qualitative synthesis (Figure). As per the GRADE
102 criteria, the included studies were appraised as moderate (Table 1). The studies were
103 both case-control studies and showed significant improvement in outcome measures
104 from LIPUS (Table 2).

105

106 **Discussion**

107 The systematic review had a strict study selection criteria to remove potential bias.
108 The two studies which met the criteria were subjected to qualitative data synthesis.
109 The experimental groups (EGs) in both studies reported significant improvement in
110 bone union rate, treatment period to bone union, and time to return to previous sports
111 activities compared to the control groups (CGs).¹⁸⁻¹⁹

112 Hideyuki Arima et al. in 2017 investigated the treatment effects of LIPUS on
113 progressive-stage spondylolysis. The study used case-control design on patients with
114 progressive-stage spondylolysis with magnetic resonance imaging (MRI). Nine
115 patients were given routine physical therapy, including avoidance of any sport activity

116 and the use of a brace during the treatment, while six patients were treated using
117 LIPUS every day during treatment in addition to routine physical therapy. About every
118 1.5 months, bone healing was evaluated via CT. Cases that retained defects after 4.5
119 months were defined as non-union. The most important finding was that the bone
120 union rate in LIPUS group was significantly higher than that in routine physical
121 therapy group (66.7 vs. 10.0%, $p=0.020$). It is a form of mechanical energy transmitted
122 into the tissue as sound waves creating series of biomechanical changes at cellular
123 level. The treatment period to bone union was 3.8 months and 2.7 ± 0.3 months in
124 routine physical therapy and LIPUS groups. The said study revealed that LIPUS
125 treatment is effective for bone union in patients with progressive-stage spondylolysis
126 with MRI high-signal change.¹⁸

127 The primary concerns of these two retrieved studies were that no randomised
128 controlled trial (RCT) for LIPUS for lumbar spondylolysis was available in literature,
129 and the two eligible studies had limited sample sizes. The actual treatment protocol
130 was not mentioned clearly. For example, details about frequency, intensity and
131 duration of trunk muscle strength and flexibility exercises were not provided. The
132 outcome measure used in the 2019 study to Masahiro et al. was time to return to
133 previous sports activities, while Hideyuki et al. set it as bone union rate and treatment
134 period to bone union.¹⁸⁻¹⁹

135 The major limitations of the current review were sample size estimation and lack of
136 RCTs in literature in the matter under review.

137 RCTs must be done to determine the role of LIPUS in the treatment of patients with
138 LBP associated with spondylolysis. Moreover, treatment effects of these studies
139 should be graphically represented through meta-analysis.

140

141 **Conclusion**

142 Only a few studies were found eligible for qualitative synthesis and were rated as
143 moderate on quality assessment through evaluation and critical appraisal which

144 concluded that LIPUS is effective for bone union and a useful therapy for quick return
145 to playing sports in patients with lumbar spondylolysis.

146

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154

155 **References**

- 156 1. Bernardelli G, Vigna L, Nava C. Physical Activity in Healthcare Workers with
157 Low Back Pain: Effects of the Back-FIT Randomized Trial. *J Occu Envi Med.*
158 2020; 62:245-9. doi:10.1097/JOM.0000000000001844.
- 159 2. Sayari AJ, Harada GK, Lopez GD. Stress Fractures of the Lumbar Spine. In
160 Stress Fractures in Athletes. 2020 (pp. 191-207). Springer, Cham.
- 161 3. Mironov SP, Cykunov MB, Burmakova GM, Andreev SV. Lumbosacral pain
162 in athletes and ballet dancers: spondylolysis and spondylolisthesis.
163 Conservative treatment. *J Trauma Ortho.* 2020; 27:11-8. doi:
164 10.17116/vto20190215
- 165 4. Tawfik S, Phan K, Mobbs RJ. The incidence of pars interarticularis defects in
166 athletes. *Global Spine J.* 2020; 10:89-101. doi: 10.1177/2192568218823695_
- 167 5. Lin T, Zhang Z, Jiang Q, Yin J. The Joe-Lin Operative Classification System
168 for Pediatric Lumbosacral Spondylolysis and Spondylolisthesis. *World*
169 *Neurosurgery.* 2020. doi: 10.1016/j.wneu.2020.05.101_
- 170 6. Wong JS, Lalam R, Cassar-Pullicino VN. Stress Injuries of the Spine in Sports.
171 *In Seminars Musculo Radio.* 2020; 24:262-276. doi: 10.1055/s-0040-1709484.

- 172 7. Koslosky E, Gendelberg D. Classification in Brief: The Meyerding
173 Classification System of Spondylolisthesis. A Publication of The Association
174 of Bone and Joint Surgeons®| CORR®. 2020; 478:1125-30. doi:
175 10.1097/CORR.0000000000001153.
- 176 8. Cambridge ED. Hip & Spine Mechanics-Understanding the linkage from
177 several perspectives of injury mechanisms to rehabilitation. Biomech Model.
178 2020; 21: 28-29.
- 179 9. Yokoe T, Tajima T, Sugimura H. Comparison of symptomatic spondylolysis in
180 young soccer and baseball players. J Ortho Surg Research. 2020; 15:1-6. doi:
181 10.1186/s13018-020-01910-4.
- 182 10. Tsukagoshi Y, Kamegaya M, Tatsumura M. Characteristics and diagnostic
183 factors associated with fresh lumbar spondylolysis in elementary school-aged
184 children. Euro Spine J. 2020; 29:2465-9. doi: 10.1007/s00586-020-06553-x.
- 185 11. Sairyo K, Sakai T, Takata Y. Spondylolysis and Spondylolisthesis in Athletes.
186 In Spinal Conditions in the Athlete. 2020 (pp. 235-247). Springer, Cham.
- 187 12. van den Heuvel MM, Oei EH, Bierma-Zeinstra SM, van Middelkoop M. The
188 prevalence of abnormalities in the pediatric spine on MRI: a systematic review
189 and meta-analysis. Spine. 2020; 45:1185-96. doi:
190 10.1097/BRS.0000000000003527.
- 191 13. Mistiaen W, Vanhecke B, Linden P. Case report: successful conservative
192 treatment of a soccer player with multiple-level spondylolysis. Current Ortho
193 Practice. 2020; 31:315-7. doi: 10.1097/BCO.0000000000000857.
- 194 14. Achar S, Yamanaka J. Back Pain in Children and Adolescents. Ameri Family
195 Phys. 2020; 102:19-28.
- 196 15. Berber R, Aziz S, Simkins J. Low Intensity Pulsed Ultrasound Therapy
197 (LIPUS): A review of evidence and potential applications in diabetics. J Clinic
198 Ortho Trauma. 2020; 11:500-505. doi: 10.1016/j.jcot.2020.03.009.

- 199 16.Chen Y, Cai Q, Pan J, Zhang D. Role and mechanism of micro-energy
 200 treatment in regenerative medicine. *Trans And Urol.* 2020; 9:690-701.
 201 doi: 10.21037/tau.2020.02.25.
- 202 17.Bull FC, Al-Ansari SS, Biddle S. World Health Organization 2020 guidelines
 203 on physical activity and sedentary behaviour. *British J Sports Med.* 2020;
 204 54:1451-62. doi: 10.1136/bjsports-2020-102955.
- 205 18.Arima H, Suzuki Y, Togawa D. Low-intensity pulsed ultrasound is effective for
 206 progressive-stage lumbar spondylolysis with MRI high-signal change. *Euro*
 207 *Spine J.* 2017; 26:3122-8. doi: 10.1007/s00586-017-5081-z.
- 208 19.Tsukada M, Takiuchi T, Watanabe K. Low-intensity pulsed ultrasound for
 209 early-stage lumbar spondylolysis in young athletes. *Clinic J Sport Med.* 2019;
 210 29:262-6. doi: 10.1097/JSM.0000000000000531.

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Table 1: Quality assessment based on GRADE criteria.

No of studies (No of participants)	Quality assessment					Summary of findings			
	Study limitations*	Consistency	Directness	Precision	Publication bias	Relative effect (95% CI)	Best estimate of effect (95% CI)	Absolute effect (95% CI)	Quality
2(95)	Serious limitations (-1)	No important inconsistency	Direct	No important imprecision	unlikely	2.7 (2.4 to 3)	66.7 %	61 days; 167 days	+++, moderate

215 GRADE: Grading of recommendations, assessment, development, and evaluations.
 216 CI: Confidence interval.

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225 **Table 2: Qualitative data synthesis of the studies reviewed.**

Study	Study Design	Groups	Outcomes	Findings	Authors conclusion
(Hideyuki, Arima et al. 2017)	Case-Control Study 13 subjects EG: 6 CG: 7	EG: low intensity pulsed ultrasound CG: cease any sport activity, wear a brace during treatment to immobilize the trunk, trunk muscle exercises and trunk flexibility exercises	Bone union rate Treatment period to bone union	EG: 66.7% CG: 10% p = 0.020 EG: 3.8 CG: 2.7±0.3	LIPUS treatment might be effective for bone union in patients with progressive-stage spondylolysis with MRI high-signal change.
(Masahiro Tsukada, PT et al. 2019)	Case-Control Study 82 subjects EG: 35 CG: 47	EG: low intensity pulsed ultrasound CG: Thoracolumbosacral brace, sports modification, and therapeutic Exercise, activity restriction, hip stretching and strengthening of the trunk muscles.	Time to return to previous sports activities	EG: 61(58-69) days CG: 167 (135-263) days P<0.01	LIPUS combined with conservative treatment for early-stage lumbar spondylolysis in young athletes could be a useful therapy for quick return to playing sports.

226 EC: Experimental group; CG: Control group; LIPUS: Low-intensity pulsed
227 ultrasound.

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231 **Figure: Study flow-chart.**

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Identification

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Screening

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Eligibility

246

Included

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