·综述·

定量超声在骨质疏松中的应用及评价

李超 齐青 董健

中图分类号：R443 文献标识码：A 文章编号：1006-7108(2011)10-0933-05

摘要：定量超声技术具有设备成本及检查费用低、无电离辐射、简便快速、可携带、可反映骨的微结构等优点，在评价松质骨状况和诊断骨质疏松症方面受到国内外医学界的高度重视。但由于骨超声仪器之间差别较大，难以进行有效的质量控制，故定量超声技术在骨质疏松方面的临床应用还存在着一些问题。本文将从技术原理、测量部位、临床价值及质量控制方面对定量超声在骨质疏松中的应用进行综述，为其进一步研究以及在临床上的推广应用奠定基础。

关键词：骨定量超声；骨密度；骨质疏松性骨折；质量控制

The application and evaluation of quantitative ultrasound in osteoporosis *LI Chao, QI Qing, DONG Jian.*

Department of Orthopedics and Department of Ultrasound, Zhongshan Hospital, Fudan University, Shanghai 200032, China
Corresponding author: DONG Jian, Email: dong.jian@zs-hospital.sh.cn

Abstract: With the advantages of low cost, no ionizing radiation, easy and convenient to use, portability, and reflecting the microstructure of bone, quantitative ultrasound has been paid high attention in assessment of cancellous bone and diagnosis of osteoporosis by medical researchers both nationally and internationally. However, the quality cannot be effectively controlled in bone quantitative ultrasound tests because of the significant differences among the bone ultrasound equipments. So there are still some problems in the clinical application of bone quantitative ultrasound. This review discusses the application of bone quantitative ultrasound in osteoporosis from its technical principles, measurement site, clinical value, and quality control, to lay the foundation for its further research and clinical application.

Key words: Bone quantitative ultrasound; Bone mineral density; Osteoporotic fracture; Quality control

骨质疏松症是以骨强度下降，骨折风险性增加为特征的骨骼系统疾病。近年来，我国正逐步向老龄化社会过渡，老年性骨质疏松症患者已接近1亿。骨质疏松症的诊断和预防成为学术界研究的热点和前沿课题[1-5]。

目前，应用于骨质疏松症的检查方法如X线检查法、双光子吸收法、双能X线吸收法(dual-energy X-ray absorptiometry, DXA)和定量CT等由于价格昂贵、耗费时间、辐射大等原因，难以广泛普及应用。而且，这些方法的测量结果只能反映骨矿密度(bone mineral density, BMD)，即"量"的因素，而不能反映"质"的因素[6,7]。然而骨质疏松性骨折的主因是骨强度下降，骨强度不仅与BMD有关，还是骨的微结构、构造等因素协同作用的结果[8-10]。基于定量超声技术(quantative ultrasound, QUS)具有设备成本低、检查费用低、无电离辐射、简便、快速、可携带、可反映骨的微结构等优点，在评价松质骨状况和诊断骨质疏松症方面受到国内外医学界的高度重视[11,12]。

本文将从技术原理、测量部位、临床价值及质量控制等方面对定量超声在骨质疏松中的应用进行综述，为其推广应用奠定基础。

1 QUS的原理

QUS测量一般采用透射法，在被测量骨的两侧各放置一个探头，一个用于发射，一个用于接收。根据探头和被测对象的接触方式分为干法和湿法。干法即探头和被测对象之间以耦合剂相接触；湿法是将两探头固定在水槽两侧，将被测对象浸泡在水中

基金项目：2010年上海市医学领军人才项目(编号:LJ10017)；上海市重点科技攻关项目"松质骨状况的超声诊断技术及系统研制"(编号:09441900400)
作者单位：200032 上海，复旦大学附属中山医院骨科
通讯作者：董健，Email:dong.jian@zs-hospital.sh.cn

进行测量。测量指标主要是超声传播速度(speed of sound, SOS)、超声宽幅衰减(broadband attenuation, BUA)以及由这两个指标计算出的其他指标如振幅相关的超声传播速度(amplitude dependent speed of sound, AD-SoS)、硬度指数(stiffness index)和定量超声指数(quantitative ultrasound index, QUI)等[13,14]。

近年来,已有学者尝试用背散射技术进行骨超声测量,采用一系列新指标如背散射系数(backscatter coefficient, BSC)[15]、频谱最大值偏移量(spectral maximum shift of ultrasonic backscatter signals, SMS)[16]及声阻抗分布(acoustic impedance, AI)[17]来评价松质骨状况,于透射法超声技术相比,能更好的反映松质骨的微结构,有着很好的应用前景。

2 测量部位

目前最常用的骨超声测量部位为跟骨。由于跟骨的松质骨含量高,能更早、更准确的预测骨质疏松和骨折风险,且跟骨有较大的平行面,周围软组织较薄,使操作在技术上更容易实现[18]。其他如指骨、桡骨及胫骨等部位的超声测量,也有所应用。还有学者尝试在髋部、腰椎等轴心部位进行超声测量,以此预测同部位的骨密度及骨折风险[19-21],这比用外周骨超声值预测髋部、椎体骨折风险更为准确,但相关技术仍不成熟,离临床应用还有一定距离。

3 临床应用

3.1 鉴别或预测骨质疏松性骨折

跟骨超声指标能将骨质疏松性髋部、椎体或其他部位的骨折患者和同年龄的非骨折对照人群有效区别开[22-26]。欧洲诺福克癌症前瞻性研究(EPIC-Norfolk)对年龄段在42~82岁的14824例被测者进行跟骨超声检测,并随访1.9±0.7年,以评估跟骨定量超声检测对骨质疏松性骨折的预测效果[27]。结果表明,跟骨定量超声对女性及男性的骨质疏松性骨折都有很好的预测效果。但该研究中,最终发生骨折的患者很少,这可能和随访时间较短有关。众多学者对跟骨超声预测骨质疏松性骨折进行了前瞻性研究。结果表明,对于髋部和椎体骨折来说,各骨超声指标每下降1个标准差所引起的相对危险度为2.0(RR/SD=2.0);对于全身所有骨折来讲,各骨超声指标每下降1个标准差所引起的相对危险度为1.5(RR/SD=1.5)。

有学者对跟骨及指骨超声检测和椎体BMD在椎体骨折的鉴别方面进行比较。结果表明跟骨及指骨超声指标和椎体BMD有着很好的相关性,超声检测在骨折鉴别方面有着和椎体BMD一样好的效果[28-31]。Krieg等[32]对70~80岁的人进行跟骨及指骨超声检测,结果也表明跟骨或指骨超声指标对鉴别椎体骨折都有着很好的效果。但跟骨超声指标的鉴别效果要比指骨超声指标更好。

近几年有学者采用新的超声技术,对股骨或椎体进行骨超声检测,体外实验结果表明尸体股骨的超声指标与其BMD有着很高的相关性,并且测量的准确度也很好[19-21,33,34]。如果类似结果在体内实验也能达到,那么这种方法将会有着广阔的应用前景。

3.2 诊断骨折疏松症或筛选骨质疏松患者

WHO根据BMD所确立的以*T*值等于或小于-2.5作为骨质疏松症诊断标准的方法对于QUS仪器并不适用[35-38]。超声仪器及测量部位不同,所得出的结果将会有很大的差异。如果以*T*值等于或小于-2.5作为诊断标准,各超声仪器或在各测量部位检测所得出的骨质疏松症患病率将会相差10倍[35,39]。到目前为止,尚无学者单用QUS结果作为骨质疏松的诊断标准。

Hans等[40,41]以QUS指标和BMD有良好的相关性为依据,用BMD作为诊断骨质疏松的金标准,选择超声指标诊断敏感性为90%点的值作为上限值,即QUI为83单位或Stiffness指数为78%的点;选择特异性为90%点的值作为下限值,即QUI为59单位或Stiffness指数为57%的点。指标大于或等于上限值的被测者基本排除患骨质疏松的可能性,指标小于或等于下限值的被测者则被诊断为骨质疏松。作者用这种方法对5954名年龄大于或等于75岁的白人女性进行诊断,最终假阳性率为13%,假阴性率为11%。指标在上限值和下限值之间的被测者则被推荐进一步做BMD检查,根据BMD结果进行诊断。但上限值和下限值的确定随骨超声仪器的不同而不同,本研究中所用的仪器为Achilles定量超声仪,所得的结果不能推广到其他仪器。上述方法结合临床危险因素(clinical risk factors, CRF)可被用于筛选骨质疏松患者,既大幅度减少被筛选人群的射线照射量,又降低了成本。

3.3 评估治疗

评估患者是否应该开始抗骨质疏松治疗主要根据患者的BMD水平。骨质疏松性骨折的发生与骨

强度密切相关,而骨强度不仅包括BMD,还与骨结构及骨转换水平等有关。QUS指标相对于BMD能更好的反映骨强度状况[42],而且QUS指标和BMD也有着很好的相关性。所以用QUS和CRF相结合理论上也可用于评定治疗的开始[43]。但目前还没有随机对照双盲的临床研究来评估这种方法的具体效果。

由于不同超声仪器的远期精确度相差很大,而且抗骨质疏松药物引起的骨质变化在外周骨可能不明显,还有许多其他的未知原因,超声在药物疗效评定方面的效果不是很好[44]。Gonnelli等[45,46]尝试用跟骨超声指标评价骨质疏松患者对抗骨吸收药物的反应,结果表明跟骨超声指标不能很好的反映药物的临床效果。

4 QUS的质量控制

各种QUS仪器在上市前都会进行准确度及精确度的评估。由于存在具体技术以及测量部位的差别,所以各仪器都有自己的测量模具。Glüer等[47]在一项欧洲多中心临床研究中曾尝试用一种超声模具来横向比较几种不同的QUS仪器(Achilles +, UBIS 5000, DTU-1, QUS-2),以进行质量控制。但其具体质量控制程序的科学性还有待验证。目前市场上还没有用于不同仪器间横向比较的统一的模具。QUS仪器的质量控制是一项十分复杂和困难的工作。

为减少测量误差,以下几方面应加以控制。

(1)测量点的位置要保持一致,如跟骨测量时每次都应测量同一点[48]。

(2)减少软组织对结果的影响。如被测者测量部位存在软组织水肿,则不宜进行干法测量[49]。

(3)减少测量温度的影响。在一定温度范围内,皮肤温度每升高1℃,SOS值就会下降3.6 m/s[50],所以测量时要保证温度一致。

(4)要选择传导性好的耦合剂,使超声能通过耦合剂经皮肤进入体内。

(5)要每天用仪器专用模具对该仪器进行测试,以便及时发现和调整仪器偏差[51]。

5 总结

QUS具有设备成本低、检查费用低、无电离辐射、简便、快速、可携带、可反映骨的微结构等优点,在骨质疏松相关的临床应用中有着广阔的前景。但目前的QUS仪器由于采用具体技术及测量部位的不同,所检测的指标存在着很大的差异。因此无法确定普遍适用的QUS指标正常值及骨质疏松诊断标准,也无法进行统一的质量控制。这些方面限制了QUS在临床上的推广应用。如果能有效解决上述问题,QUS有望替代DXA,成为早期发现骨质疏松、检测病情变化的首选工具。

【参考文献】

[1] Reginster J Y, Burlet N. Osteoporosis: A still increasing prevalence. Bone, 2006, 38Suppl. 1(2):4-9.

[2] Siffert RS, Kauftnan J J. Ultrasonic bone assessment: "The time has come". Bone, 2007, 40(1):5-8.

[3] Gluer CC. Quantitative Ultrasound - It is time to focus research efforts. Bone, 2007, 40(1):9-13.

[4] Laugier P. Quantitative ultrasound of bone: looking ahead. Joint Bone Spine, 2006, 73(2):125-128.

[5] Laugier P. Instrumentation for *in vivo* ultrasonic characterization of bone strength. IEEE Transactions on Ulatrasonics Ferroelectrics and Frequency Control, 2008, 55(6):1179-1196.

[6] Nayak S, Roberts MS, Greenspan SL. Osteoporosis Screening Preferences of Older Adults. Journal of Clinical Densitometry, 2009, 12(3):279-286.

[7] Yamauchi H, Fukunaga M, Nishikawa A, et al. Changes in distribution of bone densitometry equipment from 1996 to 2006 in Japan. Journal of Bone and Mineral Metabolism, 2010, 28(1):60-67.

[8] Swanenburg J, Adank JP, Dubs B, et al. Correlation between QUS and DXA measurements by 40-59-year-old women. Osteoporosis International, 2010, 21Suppl. 1:239.

[9] Lee HD, Hwang HF, Lin MR. Use of quantitative ultrasound for identifying low bone density in older people. Journal of Ultrasound in Medicine, 2010, 29(7):1083-1092.

[10] Guglielmi G, Adams J, Link TM. Quantitative ultrasound in the assessment of skeletal status. European Radiology, 2009, 19(8):1837-1848.

[11] Hughes ER, Leighton TG, White PR, et al. Investigation of an anisotropic tortuosity in a biot model of ultrasonic propagation in cancellous bone. Journal of the Acoustical Society of America, 2007, 121(1):568-574.

[12] Lee KI. Relationships of bone density with quantitative ultrasound parameter in bovine cancellous bone. Journal of the Korean Physical Society, 2009, 54(1):71-74.

[13] Chaffai S, Peyrin F, Nuzzo S, et al. Ultrasonic characterization of human cancellous bone using transmission and backscatter measurements: Relationships to density and microstructure. Bone, 2002, 30(1):229-237.

[14] Bauer AQ, Anderson CC, Holland MR, et al. Bone sonometry: Reducing phase aberration to improve estimates of broadband ultrasonic attenuation. Journal of the Acoustical Society of America, 2009, 125(1):522-529.

[15] Ta DA, Wang WQ, Huang K, et al. Analysis of frequency

dependence of ultrasonic backscatter coefficient in cancellous bone. Journal of the Acoustical Society of America ,2008,124(6):4083-4090.

[16] Ta DA, Zhou GH, Wang WQ, et al. Measurement of spectral maximum shift of ultrasonic backscatter signals in cancellous bone [M]. New York:IEEE,2005. ,2703-2706.

[17] 他得安,王威琪,汪源源,等.基于超声背散射信号分析松质骨中的声阻抗.中国生物医学工程学报,2007,26(4):487-492.

[18] Khaw KT, Reeve J, Luben R, et al. Prediction of total and hip fracture risk in men and women by quantitative ultrasound of the calcaneus: EPIC-Norfolk prospective population study. Lancet, 2004,363(9404):197-202.

[19] Barkmann R, Dencks S, Laugier P, et al. Femur ultrasound (FemUS)-first clinical results on hip fracture discrimination and estimation of femoral BMD. Osteoporosis International,2010,21(6):969-976.

[20] Barkmann R, Laugier P, Moser U, et al. A device for *in vivo* measurements of quantitative ultrasound variables at the human proximal femur. IEEE Transactions on Ulatrasonics Ferroelectrics and Frequency Control,2008,55(6):1197-1204.

[21] Barkmann R, Laugier P, Moser U, et al. *In vivo* measurements of ultrasound transmission through the human proximal femur. Ultrasound in Medicine and Biology,2008,34(7):1186-1190.

[22] Huopio J, Kroger H, Honkanen R, et al. Calcaneal ultrasound predicts early postmenopausal fractures as well as axial BMD. A prospective study of 422 women. Osteoporos International,2004, 15(3):190-195.

[23] Stewart A, Kumar V, Reid DM. Long-term fracture prediction by DXA and QUS: a 10-year prospective study. Journal of Bone and Mineral Research,2006,21(3):413-418.

[24] Miller PD, Siris ES, Barrett-Connor E, et al. Prediction of fracture risk in postmenopausal white women with peripheral bone densitometry: Evidence from the National Osteoporosis Risk Assessment. Journal of Bone and Mineral Research, 2002, 17(12):2222-2230.

[25] Schneider J, Bundschuh B, Spath C, et al. Discrimination of patients with and without vertebral fractures as measured by ultrasound and DXA osteodensitometry. Calcified Tissue International,2004,74(3):246-254.

[26] Mulleman D, Legroux-Gerot I, Duquesnoy B, et al. Quantitative ultrasound of bone in male osteoporosis. Osteoporos International,2002,13(5):388-393.

[27] Khaw KT, Reeve J, Luben R, et al. Prediction of total and hip fracture risk in men and women by quantitative ultrasound of the calcaneus: EPIC-Norfolk prospective population study. Lancet, 2004,363(9404):197-202.

[28] El M A, Morjane F, Mounach A, et al. Performance of calcaneus quantitative ultrasound and dual-energy X-ray absorptiometry in the discrimination of prevalent asymptomatic osteoporotic fractures in postmenopausal women. Rheumatology International,2009,29(5):551-556.

[29] Camozzi V, De Terlizzi F, Zangari M, et al. Quantitative bone ultrasound at phalanges and calcaneus in osteoporotic postmenopausal women: influence of age and measurement site. Ultrasound in Medicine and Biology,2007,33(7):1039-1045.

[30] Lappa V, Dontas IA, Trovas G, et al. Quantitative ultrasound is better correlated with bone mineral density and biochemical bone markers in elderly women. Clinical Rheumatology,2007,26(7): 1067-1073.

[31] Hartl F, Tyndall A, Kraenzlin M, et al. Discriminatory ability of quantitative ultrasound parameters and bone mineral density in a population-based sample of postmenopausal women with vertebral fractures: results of the Basel Osteoporosis Study. Journal of Bone and Mineral Research,2002,17(2):321-330.

[32] Krieg MA, Cornuz J, Ruffieux C, et al. Comparison of three bone ultrasounds for the discrimination of subjects with and without osteoporotic fractures among 7562 elderly women. Journal of Bone and Mineral Research,2003,18(7):1261-1266.

[33] Barkmann R, Laugier P, Moser U, et al. A method for the estimation of femoral bone mineral density from variables of ultrasound transmission through the human femur. Bone,2007,40(1):37-44.

[34] Dencks S, Barkmann R, Padilla F, et al. Wavelet-based signal processing of *in vitro* ultrasonic measurements at the proximal femur. Ultrasound in Medicine and Biology,2007,33(6):970-980.

[35] Damilakis J, Perisinakis K, Gourtsoyiannis N. Imaging ultrasonometry of the calcaneus: optimum T-score thresholds for the identification of osteoporotic subjects. Calcified Tissue International,2001,68(4):219-224.

[36] Wuster C, Albanese C, De Aloysio D, et al. Phalangeal osteosonogrammetry study: Age-related changes, diagnostic sensitivity, and discrimination power. Journal of Bone and Mineral Research,2000,15(8):1603-1614.

[37] Hans D, Rizzoli R, Thiebaud D, et al. Reference data in a Swiss population. Discordance in patient classification using T-scores among calcaneum, spine, and femur. Journal of Clinical Densitometry,2001,4(4):291-298.

[38] Hans D, Krieg M A. Quantitative ultrasound for the detection and management of osteoporosis. Salud Pública de México,2009, 51 Suppl 1:S25-S37.

[39] Knapp KM, Blake GM, Spector TD, et al. Can the WHO de? nition of osteoporosis be applied to multi-site axial transmission quantitative ultrasound?. Osteoporosis International, 2004, 15: 367-374.

[40] Hans D, Hartl F, Krieg MA.. Device-speci? c weighted T-score for two quantitative ultrasounds: operational propositions for the management of osteoporosis for 65 years and older women in Switzerland. Osteoporosis International,2003,14:251-258.

[41] Clowes JA, Peel NF, Eastell R. Device-speci? c thresholds to diagnose osteoporosis at the proximal femur: an approach to interpreting peripheral bone measurements in clinical practice. Osteoporosis International,2006,17:1293-1302.

(下转第 932 页)

[25] Center JR, Bliuc D, Nguyen TV, et al. Risk of subsequent fracture after low-trauma fracture in men and women. JAMA, 2007, 297:387-394.
[26] Ekman EF. The role of the orthopaedic surgeon in minimizing mortality and morbidity associated with fragility fractures. J Am Acad Orthop Surg, 2010,18(5):278-285.
[27] Kanis JA, Johnell O, De Laet C, et al. A meta-analysis of previous fracture and subsequent fracture risk. Bone,2004,35:375-386.
[28] Dominguez LJ, Scalisi R, Barbagallo M. Therapeutic options in osteoporosis. Acta Biomed, 2010,81 Suppl 1:55-65.
[29] Villareal DT, Fontana L, Weiss EP, et al. Bone mineral density response to caloric restriction-induced weight loss or exercise-induced weight loss: a randomized controlled trial. Arch Intern Med,2006, 166:2502-2512.
[30] Laliberté MC, Perreault S, Dragomir A, et al. Impact of a primary care physician workshop on osteoporosis medical practices. Osteoporos Int, 2010,21(9):1471-1485.
[31] Berg KM, Kunins, HV, Jackson, JL, et al. Association between alcohol consumption and both osteoporotic fracture and bone density. Am J Med 2008; 121:406-417.
[32] Ensrud, KE, Lui LY, Taylor BC, et al. Renal function and risk of hip and vertebral fractures in older women. Arch Intern Med, 2007, 167:133-145.
[33] Mezuk B, Eaton WW, Golden SH. Depression and osteoporosis: epidemiology and potential mediating pathways. Osteoporos Int, 2008, 19:1-12.
[34] Gerdhem P, Ivaska KK, Isaksson A, et al. Associations between homocysteine, bone turnover, BMD, mortality, and fracture risk in elderly women. J Bone Miner Res, 2007, 22:127-138.
[35] McLean RR, Jacques PF, Selhub J, et al. Plasma B vitamins, homocysteine, and their relation with bone loss and hip fracture in elderly men and women. J Clin Endocrinol Metab, 2008, 93:2206-2217.
[36] Reginster JY, Brandi ML. Fracture prevention in osteoporosis: assessing risks, providing solutions. Osteoporos Int, 2010, 21 Suppl 2:S401-S402.
[37] Tucker KL, Morita K, Qiao N, et al. Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: The Framingham Osteoporosis Study. Am J Clin Nutr, 2006, 84:936-948.
[38] Biver E, Chopin F, Coiffier G,et al. Bone turnover markers for osteoporotic status assessment? A systematic review of their diagnosis value at baseline in osteoporosis. Joint Bone Spine, 2011,1:16-23.

(收稿日期:2011-05-26)

(上接第936页)

[42] Hakulinen MA, Toyras J, Saarakkala S, et al. Ability of ultrasound backscattering to predict mechanical properties of bovine trabecular bone. Ultrasound in Medicine and Biology, 2004,30(7):919-927.
[43] Krieg MA, Barkmann R, Gonnelli S, et al. Quantitative ultrasound in the management of osteoporosis: The 2007 ISCD Official Positions. Journal of Clinical Densitometry, 2008, 11 (1):163-187.
[44] Hans D, Krieg MA. The clinical use of quantitative ultra-sound (QUS) in the detection and management of osteoporosis. IEEE Transactions on Ulatrasonics Ferroelectrics and Frequency Control,2008,55(7):1529-1538.
[45] Gonnelli S, Cepollaro C, Montagnani A, et al. Alendronate treatment in men with primary osteoporosis: a three-year longitudinal study. Calcified Tissue International,2003,73:133-139.
[46] Gonnelli S, Cepollaro C, Montagnani A, et al. Heel ultrasonography in monitoring alendronate therapy: a four-year longitudinal study. Osteoporosis International, 2002, 13: 415-421.
[47] Glüer CC, Eastell R, Reid DM, et al. Association of ? ve quantitative ultrasound devices and bone densitometry with osteoporotic vertebral frac-tures in a population-based sample: the OPUS Study. Journal of Bone and Mineral Research,2004,19 (5):782-793.
[48] Laugier P, Giat P, Berger G. Broadband ultrasonic attenuation imaging: a new imaging technique of the os calcis. Calcified Tissue International,1994,54(2):83-86.
[49] Johansen A, Stone MD. The effect of ankle oedema on bone ultrasound assessment at the heel. Osteoporosis International, 1997,7(1):44-47.
[50] Paggiosi MA, Blumsohn A, Barkmann R, et al. Effect of temperature on the longitudinal variability of quantitative ultrasound variables. Journal of Clinical Densitometry,2005,8 (4):436-444.
[51] Hans D, Wacker W, Genton L, et al. Longitudinal quality control methodology for the quantitative ultrasound Achilles plus in clinical trial settings. Osteoporosis International, 2002, 13 (10):788-795.

(收稿日期:2011-11-22)

定量超声在骨质疏松中的应用及评价

作者：　李超， 齐青， 董健， LI Chao， QI Qing， DONG Jian
作者单位：　复旦大学附属中山医院骨科,上海,200032
刊名：　中国骨质疏松杂志 ISTIC
英文刊名：　Chinese Journal of Osteoporosis
年，卷(期)：　2011,17(10)