REVIEW ARTICLE

Quantitative Ultrasound (QUS) for the Assessment of Bone Health

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ABSTRAK

Osteoporosis dikenali sebagai penyakit senyap kerana tidak mempunyai tanda-tanda awal. Ini disebabkan oleh kepadatan tulang yang berkurangan secara perlahan-lahan seiring dengan peningkatan usia. Insiden penyakit ini semakin meningkat setiap tahun di seluruh dunia. Mengukur ketumpatan mineral tulang (BMD) menggunakan densitometry tulang konvensional (DXA) adalah praktikal dalam diagnosis osteoporosis tetapi kosnya adalah tinggi dan tidak dapat dilaksanakan dalam masyarakat. Untuk mengukur ketumpatan tulang, "quantitative ultrasound" (QUS) adalah teknik yang agak moden untuk diagnosis osteoporosis. Ianya agak mudah, konsisten, lebih murah dan kaedah yang selamat berbanding dengan teknik densitometry yang lain. Kedua-dua parameter QUS yang diukur pada masa kini adalah ultrasound jalur pengecilan (BUA) dan kelajuan bunyi (SOS). QUS juga dapat menjangka risiko patah. Ianya kini digunakan untuk memantau tindakbalas kepada rawatan anti-osteoporosis. Kajian in-vitro menunjukkan bahawa indeks QUS berhubungkait dengan BMD, bentuk tulang mikro dan parameter mekanikal. Oleh yang demikian, QUS berupaya untuk menjadi teknik baru untuk penilaian tulang.

Kata kunci: quantitative ultrasounds (QUS), dual energy X-ray (DXA), ketumpatan tulang, osteoporosis

ABSTRACT

Osteoporosis is known as a silent disease because bone density slowly decreases with advancing age and without symptoms. The incidence of osteoporosis is increasing yearly worldwide. Measuring bone mineral density (BMD) using conventional bone densitometry (DXA) is practical in diagnosis of osteoporosis but the cost is high and cannot be implemented in community. However, quantitative

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ultrasound (QUS) is a modern technique to measure the bone density and also for the diagnosis of osteoporosis. It is comparatively easy, reliable, less costly, and a safe method compared to other techniques. QUS consists of two main parameters which are known as broadband ultrasound attenuation (BUA) and speed of sound (SOS). QUS can also predict fracture risk of BMD. QUS showed significantly associated with BMD, bone micro architecture and mechanical parameters for In vitro studies and in human studies, QUS were found to be associated with BMD. Hence, QUS is capable to be new technique for bone assessment.

Keywords: quantitative ultrasounds (QUS), dual energy x-ray (DXA), bone density, osteoporosis

INTRODUCTION

Bone is a highly metabolic tissue where it functioning as providing balance to the body, protect the inner organs and also play a role as calcium storage. It is a compound of hydroxyapatite (45%), type I collagen (40%), and water (15%). Structure level of cortical bone and trabecular bone are differ (Eckstein et al. 2007). Bone continuously models and remodels. In the cellular level, the modeling and remodeling process are not very differing. Because it is based on the separate actions of bone resorbing cells that are called osteoclasts, while bone forming cells is called osteoblasts. Bone formation exceeds bone remodeling in young individuals where the peak bone mass (PBM) is reached around the age of 20-30 years (Hara et al. 2001; Kohrt et al. 2004). The remodeling development is influenced by hormones where when the person become ageing, the level of estrogen and testosterone decrease, and will decrease bone remodeling for bone formation. In adults, peak bone mass, rate and amount of bone loss is a determinant of bone mass (Eckstein et al. 2007).

THE RISING INCIDENCE OF OSTEOPOROSIS

Osteoporosis is known as a silent disease because bone density slowly decrease with advancing age and without symptoms (Naina Mohamed et al. 2012). Osteoporosis is a progressive skeletal disease that can be described by weakening of bone and low bone density andwhich becomes clinically obvious when there is a fracture (Mcclung 2003). There are two major risk factors for osteoporotic fractures which are age and bone mineral density (BMD) (Hui et al. 1988). Osteoporosis in developing countries is on the rise (Handa and Kalla 2008). This disease causes major problems in terms of the cost to society and the cost to suffering individuals where it results in a significant increase in healthcare cost (Loh & Shong 2007). Every year, the incidence of osteoporosis and osteoporosis fracture rise with an aging society. In 1996, the elderly population (more than 50 years old) in Malaysia was approximately 2.45 million (Lee & Khir 2007) and it increased to 4.52 million in 2010 (Department of Statistics 2010). In 1997, the cost for hospitalization

Table 1: Estimated number of osteoporotic fractures by site in men and women with age more than 50 years in 2004 by World Health Organization Technical Report Series

WHO region	Sites			
	Hip	Spine	Humerus	Forearm
Africa	8	12	6	16
Americas	311	214	111	248
South-East Asia	221	253	121	306
Europe	620	490	250	574
Eastern Mediterranean	35	43	21	52
Western Pacific	432	405	197	464
Total	1672	1416	706	1660

because of hip fracture was estimated at Ringgit Malaysia 22 million, with high individual cost which many could not afford (Malaysia Osteoporosis Society 2006). Osteoporosis is one of the most important public health issues that affects the elderly in many countries, including developing countries like Malaysia.

In Malaysia, the incidence of hip fracture among individuals over 50 years of age is 0.9/1000 individuals with the highest being in Chinese women (Malaysia Osteoporosis Society 2001). Ethnicity is one of the factor to determine and influence BMD. Black and Asian women showed low BMD within each age group (Handa & Kalla 2008). It is expected that the incidence of osteoporosis is increasing rapidly in ageing population. Statistics in Malaysia showed that the percentage of population aged above 65 years grows at the rate of 3% yearly and by the year 2020 there would be 7.3% or 2 million elderly people in the country (Department of Statistic 2010).

According to the criteria set by the World Health Organization, an individual is diagnosed as osteoporotic if his or her BMD is 2.5 standard deviations (SDs) below that of a healthy young adult of the reference population or more commonly expressed as a T-score of -2.5 or less (World Health Organization 1994). Several parts or a site in our body are associated with fragility fractures which includes the hip, wrist, vertebra and rib (Yeap et al. 2012). Based on the report by the World Health Organization, 2004, it is estimated that 4.5 million people suffered from an osteoporotic fracture in America and Europe. Table 1 shows the estimated number of osteoporotic fractures by site in men and women with age more than 50 years in 2000 by the World Health Organization (World Health Organization 2004).

BONE HEALTH SCREENING FOR EARLY DETECTIONAND PREVENTION OF OSTEOPOROSIS

In order to prevent the progression to osteoporosis, early detection of bone density loss is very important (Laugier 2004). Bone densitometry is currently

used to classify individuals at greatest risk of fracture and to diagnose osteoporosis so that they can be informed that they have osteoporosis and early treatment can be initiated (Kanis & Glüer 2000). Bone loss can be assessed by several bone-densitometry methods; Dual-energy x-ray absorptiometry (DXA), quantitative computed tomography (CT), peripheral quantitative computed tomography (QCT), magnetic resonance imaging of plain films (Radiogrammetry), and quantitative ultrasound (QUS). Each tool provides distinct advantages and disadvantages which depend on the purpose or outcome of its application (Bachrach & Sills 2011).

The diagnosis of osteoporosis depends on the assessment of two bone properties. Those are bone quantity with bone mass expressed as bone mineral density (BMD) and bone quality reflectto micro-architecture properties of the bone. Bone mineral density (BMD) is the main clinical assessment to assess bone mass. Therefore, measurement of bone mass using bone densitometry form the basis for the diagnosis of osteoporosis (Kanis et al. 1997). Bone mineral density (BMD) is defined as an index of bone mass derived from the amount of mineral measured per unit area or volume of bone tissue (Kanis 2002).

BONE DENSITOMETRY: QUS AS AN ALTERNATIVE TO DXA

In measuring bone mineral density (BMD), the current gold standard for detecting osteoporosis is using dual-energy X-ray absorptiometry (DXA) (Laugier 2004). However, there are anumber of disadvantages in the use of the DXA, which include lack of the equipment, high cost, importability, and ionizing production (Laugier 2004) which limits its application for large population bone health screening programmed.

There is a wide growing interest in the use of quantitative ultrasound (QUS) amongst various technologies, for screening purposes. Quantitative ultrasound (QUS) of bone was introduced approximately two decades (1984) ago as a device for examining bone tissue (Laugier 2004) and as potential technologies in managing osteoporosis. This new health technology has attracted extensive scientific and clinical interestwhere Quantitative ultrasound (QUS) is a new method that is free from radiation, non-invasive, portable and cheaper compare to Dual X-ray Absorptiometry (DXA) (Laugier 2004). QUS scanners gives benefits to patients and doctors in the assessment of osteoporosis (Kanis & Glüer 2000). Quantitative ultrasound (QUS) evaluation of bone health status has gained popularity in recent years, especially in regions with limited access to dual X-ray absorptiometry (DXA) device. As an alternative to DXA for osteoporosis screening, quantitative ultrasound technology has gained acceptance and is currently being investigated as a tool that can replace DXA (Chin et al. 2012). Quantitative ultrasound is a useful tool for a clinical study which gives useful information about bone status and very effective in the management of patients (Guglielmi & Terlizzi 2009).

TECHNICAL ASPECTS OF QUS

There are two types of QUS, (Chin & Ima-Nirwana 2013) depending on the type of the ultrasound transmission travelling through the bone. First is axial or horizontal transmission of the ultrasound waves which travel along the cortical layer of the phalanges, radius or tibia segment of the bone. Second is the transverse or longitudinal transmission of the ultrasound waves which travel either through trabecular bone or cortical bone.

According to official International Society for Clinical Densitometry (ISCD) in 2007, the committee stated that for clinical use of QUS, calcaneal is the only validated skeletal site for the management of osteoporosis (Krieg et al. 2008). Prospective study was conducted to validate QUS against DXA for ability to predict osteoporosis fracture risk and results demonstrated that calcaneal QUS by transverse transmission devices predicts fracture accurately and better compared toother QUS devices at other skeletal sites such as the cortical phalange, and cortical radius devices (Krieg et al. 2008). Trabecular bone can be found highly at calcaneal site while some other sites of measurement are primarily cortical. The coefficient of variation can appear particularly good for cortical sites due to the higher speed of sound (SOS) in cortical bone compared to trabecular bone when measuring the SOS. It can be concluded that calcaneus QUS measurement is able to predict hip fractures and all osteoporotic fractures in elderly woman and man with similar performance to hip DXA measurements (Stewart et al. 2006). Besides, the calcaneus possesses two lateral surfaces and consists of 95% trabecular bone, which helps the movement of ultrasound through it where it is easily accessible. Furthermore, calcaneum has medial and lateral aspects being relatively flat and parallel, with a high metabolic turnover rate and a pattern of bone loss similar to the spine (Knapp 2009).

There are several parameters generated by QUS. The panel from International Society of Clinical Densitometry (ISCD) has rated the following indices as appropriate terminology (Krieg et al. 2008) and as the accepted outcome measures for calcaneal QUS devices:

1. Recommended attenuation parameter: Broadband Ultrasound Attenuation (BUA) expressed in dB/MHz,
2. Recommended velocity parameter: Speed of Sound (SOS) expressed in meters per second (m/s),
3. Composite parameter: Stiffness Index (SI) or Quantitative Ultrasound Index (QUI) is generated by combining BUA and SOS. These two composite parameters may be clinically useful in the determination of subjects having low bone health status (Chin & Ima-Nirwana 2013).

The speed of sound (SOS) refers to the division of transmission time of the sound waves by the length of the body part studied. Unit used in the SOS measurement is meter per second (m/s). Broadband attenuation (BUA) of sound refers to the slope between attenuation of sound signals and its frequency, The

unit used is dB/MHz. Soft tissue and bone absorbs energy when the sound wave undergo them, thus attenuation occurs. In recent times, latest QUS indices derived from at least two basic measurements such as amplitude-depend SOS (AD-SOS), stiffness index (SI), quantitative ultrasound index (QUI) and estimated BMD (eBMD) (Chin & Ima-Nirwana 2013). Several previous study in the past have examined the usefulness of QUS and its potential role in the field of osteoporosis whereboth broadband ultrasound attenuation (BUA) and speed of sound (SOS) measurements at the calcaneus can be used to identify individualswho are at risk of osteoporotic fracture as reliably as BMD (Bauer et al. 1997; Frost et al. 2001; Hans et al. 1996).

THE APPLICATION OF QUANTITATIVE ULTRASOUND (QUS)

The WHO T-score diagnostic classification derived from DXA measurement either at spine, hip or forearm cannot be applied to T-score derived from non-DXA measurements such as QUS because both measurements employs different technology in assessing individuals bone health status. Furthermore, it is impossible to apply the WHO T-score to other skeletal sites without having significant discrepancies.However, previous studies have demonstrated significant correlation between calcaneal QUS parameters with BMD (Dane et al. 2008; Töyräs et al. 2002) and skeletal site-matched bone mass assessed by DXA or peripheral DXA (Krieg et al. 2008). Subsequently, one could classify individuals into respective risk groups (the likelihood of having osteoporosis) by calculating the specific upper and lower threshold concept to QUS. Unlike DXA which centre its assessment only on bone mass, QUS not only measures bone mass but also measures other bone properties of bone strength which reflect bone micro architecture and material properties (Laugier 2004) (Trimpou et al. 2010) (Stewart et al. 2006). QUS is affordable, inexpensive, widely available, easy, fast, and transportable and most importantly does not produce any radiation, thus suitable to be used for large epidemiological bone health study.

Two meta-analysis on fracture risk assessment using QUS by Marin and Moayerri (Marin et al. 2006) (Moayyeri et al. 2012) provide a concrete conclusion that QUS parameters are able to predict fracture risk as good as central DXA. Previous studies have demonstrated that assessment of QUS at the calcaneal site is able to predict fracture in postmenopausal women (Kanis 2002). The ability of QUS to predict fracture was also proven in elderly men and QUS has the capability to discriminate between male and female subjects (Chin et al. 2013) at various skeletal sites and independently of the BMD assessed by central DXA. Generally, QUS has the ability to discriminate those with osteoporotic fractures (fracture at either hip, spine or any osteoporotic fractures) and those without osteoporotic fracture (Krieg et al. 2008). Furthermore, QUS overcomes the limitation by offering an

opportunity for bone health assessment particularly to people without access to DXA scanning. It is also highly suitable for use in fragile populations such as children, pregnant mothers and remote access populations.

Several studies have proved that calcaneal trabecular transmission QUS parameters are highly associated with BMD measured by DXA In human studies, SOS was found to be significantly correlated with BMD at various skeletal sites as assessed by Dane and colleagues in a cross-sectional study in 2008 (Dane et al. 2008) and by monitoring the changes of DXA and QUS at first screening and during the seven year follow-up period in a longitudinal study by Trimpou et al. in 2010. Therefore, from these two studies, it can be concluded that QUS parameters positively correlates with both BMD and BMC measured using the DXA machine. Thus, long term precisions by QUS need to be established by several large human cohort studies for the purpose of generalizing heel QUS in monitoring treatments.

BUA and SOS measurements gives indication for osteoporosis, and. Therefore, calcaneal QUS could become an alternative tool in identifying individuals who have low bone mass and possible candidates for therapeutic intervention (Frost et al. 2001). The precision of QUS is high, which make the device to be used in epidemiological studies (Trimpou et al. 2010). Some practitioners use the QUS as an indicator of risk of fracture as for example individuals who are at high risk, medium risk, or low risk, where it is dependent on the QUS parameters and also the presence of strong clinical risk factors (Stewart et al. 2006). Risk of osteoporotic fractures also can be identified in the community in postmenopausal women, as an improved process of targeting women for axial DXA BMD measurement to diagnose osteoporosis, with care, to target antiresorptive treatments when low QUS measurements are present, in addition to major clinical risk factors (Stewart & Reid 2002).

QUANTITATIVE ULTRASOUND (QUS) AND MEASUREMENT OF BONE PROPERTIES

QUS is capable in measuring micro-architectural and the density of bones (Gluer et al. 1994; Njeh et al. 2001). In-vitro studies shows that the ultrasound derived modulus of elasticity and correlates strongly with values of bone breaking strength derived from static loading (Turner & Eich 1991). In addition, a study reported that QUS parameters are significantly associated with bone structure independently of BMD (Gluer et al. 1994). As measured by mechanical testing, Mehta et al. reported ultrasound velocity and elasticity strongly connected with material elasticity (Mehta et al. 1998). Broadband ultrasound attenuation (BUA) values showed to be dependent upon trabecular orientation in vitro (Gluer et al. 1994). However, using QUS and DXA in-vivo, there was high correlation of r=0.75 to r=0.90 between BUA and BMD at the calcaneus with matched regions of interest, suggesting that QUS may reflect micro-architecture. Njeh et

al. (2001) in a review of whether QUS is dependent on structure concluded that ultrasound attenuation is due to structural parameters as well as dependent on density (Njeh et al. (2001).

The much strength of QUS does not exempt it from weaknesses. Different QUS devices made by different manufacturers employ diverse technologies and thus, different devices from different producer have different indices calculation algorithms. This is further complicated by difference in types of model, different skeletal sites of measurements and analysis and different calibration methods. As a result, bone density measurements by QUS from different manufactures and models will have significant differences and therefore cannot be directly compared. Comparison to various DXA devices with different manufactures and models is also not possible and cannot be performed due to differences in their calculation even though all DXA instruments use absolute BMD values as the common outcome measure (Krieg et al. 2008). In terms of precision, QUS has less precision when compared to DXA (Ravaud et al. 1999). Broadband ultrasound attenuation precision also appears to be poorer than its corresponding SOS precision in the same device. As a result of the poor precision of QUS in comparison to DXA, optimization of measurements to reduce precision errors is of greatest importance (Knapp 2009).

CONCLUSION

To conclude, QUS is sensitive to age and menopause-related changes, clinical risk factors and lifestyle factors related to osteoporosis. QUS and DXA have been shown to be predictive of osteoporotic fractures, especially in the elderly. QUS has been widely researched upon and has been demonstrated to have the capability to predict fracture, particularly at the hip. QUS also can be used as a screening tool for bone health, for assessment of risk of fracture in the community in postmenopausal women, as an improved method of targeting women for axial DXA BMD measurement to diagnose osteoporosis, and also to target antiresorptive treatments when low QUS measurements are present in addition to major clinical risk factors (Stewart & Reid 2002).

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