The indications of bone mineral density (BMD) measurement in the Endocrinology outpatient department

A Thesis

By

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SUMMARY

THE INDICATIONS OF BONE MINERAL DENSITY MEASUREMENT IN THE ENDOCRINOLOGY OUTPATIENT DEPARTMENT

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Aim of the study: The aim of this thesis is to evaluate and disclose the appliance of guidelines and practical recommendations regarding bone mineral density (BMD) measurements by DXA in accordance to the established 2015 International Society of Clinical Densitometry (ISCD) official positions in patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences.

Objectives:

1. Assess the correct patient’s position during examination in DXA scans according to the guidelines of the ISCD.
2. Assess the indications for BMD measurement.
3. Assess the correlation between age, sex, weight, height and BMD measurement results in women and men.
4. Assess the BMD correlation between breast cancer patients on current treatment with aromatase inhibitors (AI) (relevant as a significant risk factor for BMD decrease) and patients without breast cancer.
5. Assess the BMD measurement results in patients aged > 65 years in the category of normal weight patients and underweight patients (significant risk factor for falls and suspicion of sarcopenia).

Methods: Retrospective data among patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences has been collected and evaluated on the basis of bone density measurement values. The files collected are strictly from the year of 2016 and were collected anonymously. A sample of 102 files has been collected (Mage = 72,54, SDage = 5,72, 85,3% of which are females and 14,7% of which are males). The DXA measurements which have been carried out in the year of 2016 in the Lithuanian University of Health Sciences were done according to the guidelines of the International Society for Clinical Densitometry (ISCD) in two skeletal sides of measurement: the lumbar spine and the proximal femur (neck and total hip).
The statistical analysis was conducted using SPSS 20.0. Differences between groups were counted as significant when $p<0.05$.

**Results:**

1. In all of the researched individuals in which DXA measurements have been performed, the DXA performance has been done according to the “International Society for Clinical Densitometry (ISCD)” recommendations.
   - In 100% of selected DXA reports the technologist’s positioning and radiological analysis were performed according to the recommendations.
   - 100% of selected patients for DXA measurements have been selected according to the recommendations of the “International Society for Clinical Densitometry (ISCD)”.
   - 15 male patients > 70 years of age and in 87 female patients > 65 years of age, with a distribution of bone densitometry results of 30% for osteopenia and 70% of osteoporosis in research individuals.
   - Postmenopausal female patients represent the largest group in which BMD measurements have been conducted.
   - 38% of the research individuals are underweight (BMI < 18.5 kg/m²).

2. Age, sex and body weight composition does have significance on the presence of osteoporosis ($p<0.05$).

3. Underweight patients > 65 years of age suffering from osteoporosis disclose a significant negative T-score alteration in the spine and proximal femur (neck and total hip), $p < 0.05$.

4. Men (> 70 years of age) disclose a T-score mean values in the spine of -2.9 and hip of -2.9.

5. Women (> 65 years of age) disclose a T-score mean value in the hip of -2.9.

6. Underweight patients (> 65 years of age) disclose a T-score mean value in the spine of -2.7.

7. Breast cancer patients on aromatase inhibitor (AI) treatment disclose a T-score mean value in the spine of -3.9.

**Conclusion:**

1. All the conducted BMD measurements by DXA (indications, technologist’s positioning and radiological analysis) among patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences have been performed according to the International Society for Clinical Densitometry (ISCD) recommendations.

2. Osteopenia was determined in 30% of research individuals and osteoporosis was determined in 70% of research individuals (15 male patients > 70 years of age and 87 female patients).

3. 38% of research individuals are underweight (BMI <18.5 kg/m²).
4. Breast cancer patients on current aromatase inhibitor (AI) treatment meet the age, sex and pharmacologic therapy criterion regarding the International Society for Clinical Densitometry (ISCD).

5. Underweight in addition to suspicion of sarcopenia does represent a significantly high risk factor in fracture and falling risk.

**Recommendations:**

1. BMD measurements are necessary to be done according to the ISCD recommendations.

2. BMD measurements are necessary to be conducted in elderly individuals who suffer from underweight and where sarcopenia is suspected.

3. BMD measurement should be performed in 2 skeletal sides, namely the lumbar spine and proximal femur.

4. Fall prevention and taking preventive measures including fall avoidance and risk factor avoidance should be strictly applied, thus by decreasing future fractures; preventive measures are to be taken and recommended without diagnosis of osteoporosis.

5. Assessment of risk of falls and their prevention, including maintenance of mobility and correction of nutritional deficiencies, particularly of calcium, vitamin D and protein, should be advised and are to be strictly encouraged.
ACKNOWLEDGEMENT

I would like to thank my scientific thesis supervisor Assoc. Prof. Dr. Aurelija Krasauskienė, MD. PhD, of the Lithuanian University of Health Sciences, Faculty of Endocrinology.
Her office has always been open whenever I had questions about my research or writing. She consistently encouraged me to think for myself and imposed this paper to be my own. It has not been easy, but I am deeply thankful for the personal and academic growth I achieved through this work.

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Philippians 4:6-7

“6 Do not be anxious about anything, but in every situation, by prayer and petition, with thanksgiving, present your requests to God. 7 And the peace of God, which transcends all understanding, will guard your hearts and your minds in Christ Jesus.”

Oliver Andreas Kuratli
CONFLICTS OF INTEREST

The author reports no conflicts of interest.
ETHICS COMMITTEE CLEARANCE

Department of Bioethics of the Lithuanian University of Health Sciences has granted approval on the 2016-09-03, Nr. BEC-MF-05

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ABBREVIATIONS

AI (Aromatase inhibitor)
ASMBR (The American Society for Bone and Mineral Research)
BMD (Bone Mineral Density)
BMI (Body Mass Index)
DXA (Dual-energy X-ray absorptiometry)
ISCD (International Society for Clinical Densitometry)
INTRODUCTION

Osteoporosis is characterized as a systemic skeletal disease in which gradual degradation and microarchitectural changes of the bone mass take place, with a resulting increase of bone fragility and fracture. Individuals are predisposed to osteoporotic fractures, commonly in the spine, hip, distal forearm and proximal humerus. [1] Bone mass is lost, when the rate of resorption is higher than that of bone synthesis, like it is the case in postmenopausal osteoporosis. [2]

Risk factors associated with osteoporotic fractures include low peak bone mass, hormonal aspects, regular use of certain pharmacological substances (e.g. glucocorticoids, aromatase inhibitors (AI) in breast cancer patients), smoking, decreased physical activity, low BMI, low intake of calcium and vitamin D, small body stature and of course genetic predisposition, like family history. Approximately 200 million women have osteoporosis worldwide, with rising tendency. The possibility of developing osteoporosis is highest in North America and Europe, but developing countries and its population are at increased risk, since population longevity and life expectancy continues to rise.

Bone mineral density (BMD) measurement is the preferred diagnostic method for patients at risk of osteoporosis and is used in the antifracture treatment. The method of testing is by the use of DXA scans of the central skeleton in order to measure the BMD of the lumbar spine and hip.

Clinical indications vs. clinical questions:

1. Does my patient have osteoporosis?
2. Is my patient at sufficient fracture risk for treatment?
3. Is my patient responding to treatment?
4. Is my patient responding to therapy?
5. What does this mean?
   • Fracture on therapy?
   • Loss of BMD on the therapy?
   • What is a significant loss?
   • Is increase on therapy real? Reasonable?
   • Is a significant gain or loss different, depending on therapy?
The DXA report has to be performed by:

- Clinician
- Technologist
- Interpreter
- All working together, but more than 90% of DXA examinations/reports present one or more errors.

Every individual performing a DXA report has to do his/her task in the most professional and accurate way possible. The clinician has to order the DXA scan according the indications to measure BMD, the technologist has to deal with positioning and analysis. In the ASBMR meeting of 2016, the main subject regarding the crisis in osteoporosis was due to the decrease in the rates of testing, diagnosis, and treatment of high-risk osteoporotic patients.

Main causes are as followed:

1. Side effects of long-term suppression treatment, such as atypical femoral fracture and osteonecrosis of the jaw.
2. Poor quality of DXA scan reports leading to adverse clinical outcomes

The practical implications of ISCD recommendations is the best way to assure good quality DXA scans in which the clinician is able to trust.
AIM AND OBJECTIVES

Aim of the study:
The aim of this thesis is to evaluate and disclose the equivalent appliance of “The International Society for Clinical Densitometry (ISCD)” practical implementations of the 2015 guidelines positions for bone mineral density (BMD) measurements obtained by DXA among patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences

Objectives:
1. Assess the correct patient’s radiographic examination position according to the guidelines of the ISCD during BMD.
2. Assess the indications for BMD measurement
3. Assess the correlation between age, sex, weight, height and BMD measurement results in women and men.
4. Assess the BMD correlation between breast cancer patients on current treatment with aromatase inhibitors (AI) (relevant as a significant risk factor for BMD decrease) and patients without breast cancer.
5. Assess the BMD measurement results in patients aged > 65 years in the category of normal weight patients and underweight patients (significant risk factor for falls and prevalence of sarcopenia).
LITERATURE REVIEW

1.1 Accuracy, mistakes and importance of patient’s positioning during the performance of DXA measurements

Bone mineral density (BMD) testing is used in order to diagnose osteoporosis, to assess fracture risk and monitor changes in BMD. A variety of devices and technologies are applied to measure BMD or other surrogate markers of bone strength and vitality. Measurements obtained with these devices are often reported according to different proprietary standards, and the comparability of values obtained with different instruments, thus resulting in poor results. There is a high degree of variability in the skills of the technologists performing the tests and the clinicians interpreting and evaluating the results.

A recent survey examined the perceptions and satisfaction of the quality of DXA reports among almost 6,000 members of the International Society for Clinical Densitometry (ISCD), a non-profit professional society devoted to the advancement of excellence in the assessment of skeletal health. Responses were received from 21% of clinicians (743 of 3,488) and 32% of technologists (754 of 2,362) to whom surveys were distributed. Clinicians (71%) and a large number of technologists (45%) reported viewing an incorrect DXA interpretation at least once a month. Almost all the clinicians (98%) felt that poor-quality DXA reports were harmful and endangering to patient care. Technologists commonly experienced that demographic information and data (e.g. age or sex) had been entered incorrectly before the DXA scan, potentially resulting in a misleading or simply incorrect report. [32]

To compare serial BMD studies on the same device, precision assessment conducted according to well-recognized standards is necessary in order to calculate the precision error and least significant change (LSC). Precision error is inherent in the BMD measurement itself and is largely dependent on the skill of the technologist in placing the patient in the same body position for different scans. “Precision represents the reproducibility of the BMD measurement and is typically calculated by measuring BMD in 15 patients three times or 30 patients twice on the same day, repositioning the patient after each scan. The LSC, a value that is derived from the precision calculation, is the smallest BMD change that is statistically significant with a 95% level of confidence. Unfortunately, many DXA facilities have not done precision assessment, and quantitative comparison of BMD measurements cannot, therefore, be performed. Furthermore, there is often a lack of adherence to manufacturers’ recommendations for device maintenance and quality control, and the education and training of bone densitometry technologists and interpreters varies widely.”
Correct positioning, which primarily depends on the skill of the technologist, is critically important and a deciding factor in obtaining a valid BMD study report. The spine must be positioned in the middle of the table, parallel to the long edges of the table and visible benchmarks to help with labeling vertebral bodies. The L4–L5 interspace is usually at the level of the pelvic brim, and L1 is typically, though not always, the vertebral body below the lowest ribs associated with T12. The bone images can be used in order to check that the patient is correctly situated.

The hip should be internally rotated approximately 15°, as suggested by a small or absent protuberance of the lesser trochanter, and the shaft of the femur should be positioned parallelly to the long edge of the table unless otherwise recommended by the manufacturer. For serial BMD tests, it is critical that patient’s positioning is as similar as possible to previous ones. The ‘scan mode’ should be correctly selected for the size of the patient and BMD; a larger patient with denser bones may require a scan mode with an increased scan time than a smaller patient with less dense bones. [32]

Lumbar spine: Optimal positioning

- Spine is centered
- Spine is straight
- Not tilted
- Both iliac crests are visible
- Scan includes:
  - Middle of L5
  - Middle of T12

Femur optimal positioning:

- Straight femoral shaft
- Correct femoral rotation
- Greater trochanter centered vertically in the scan field
- No artifacts
### Table 1
Common mistakes in BMD testing.

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>MISTAKE</th>
<th>EXAMPLES/COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>INDICATION</td>
<td>Not doing bone density test in a high-risk patient</td>
<td>Healthy 67-year-old woman not tested</td>
</tr>
<tr>
<td></td>
<td>Doing bone density test when it is unlikely to change clinical management</td>
<td>Healthy 35-year-old woman is tested</td>
</tr>
<tr>
<td>QUALITY CONTROL</td>
<td>Failure to follow manufacturers’ recommendations for system maintenance and phantom measurement</td>
<td>Phantom scanning never done</td>
</tr>
<tr>
<td></td>
<td>Failure to identify and correct significant change in calibration</td>
<td>Results of phantom scanning not reviewed or instrument servicing not requested when calibration has changed</td>
</tr>
<tr>
<td></td>
<td>Failure to do precision assessment and calculate LSC</td>
<td>It is not possible to quantitatively compare BMD tests if LSC is not known</td>
</tr>
<tr>
<td>ACQUISITION</td>
<td>Improper patient positioning</td>
<td>Spine not parallel to edges of DXA table or hip not sufficiently internally rotated</td>
</tr>
<tr>
<td></td>
<td>Wrong scan mode</td>
<td>Scan mode may alter BMD and is manually or automatically selected, depending on the instrument used</td>
</tr>
<tr>
<td></td>
<td>Invalid skeletal site</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Artifacts not removed from scanned area</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Incorrect demographic information</td>
<td>BMD measured at hip with total hip replacement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spine scanned when patient is wearing underwired bra or has belly button ring in place</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Man entered as woman, or incorrect age used</td>
</tr>
<tr>
<td>ANALYSIS</td>
<td>Failure to review and correct improper default identification of bone edges and regions of interest.</td>
<td>Computer includes large osteophyte in area of measured spine. Helpful markers are the iliac crest, usually at the L4–L5 interspace, and lowest set of ribs, usually at T12</td>
</tr>
<tr>
<td>INTERPRETATION</td>
<td>Reporting T-scores in a healthy premenopausal woman and applying the WHO diagnostic criteria may result in faulty assessment of fracture risk</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Incorrect labeling of vertebral bodies</td>
<td>LSC not known, different instruments used, different bone area scanned, different labeling of vertebral bodies, left hip compared with right hip, comparing T-scores instead of BMD, different scan modes</td>
<td></td>
</tr>
<tr>
<td>Incorrect application of WHO diagnostic T-score</td>
<td>Bone loss can only be identified when serial BMD tests have been done and the LSC is known</td>
<td></td>
</tr>
<tr>
<td>criteria and ISCD Official Positions</td>
<td>Expressing fracture risk as relative risk will overestimate fracture probability if the comparator population is at low fracture risk</td>
<td></td>
</tr>
<tr>
<td>Invalid BMD comparison</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stating that bone has been lost when there is only one BMD test</td>
<td></td>
<td></td>
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<tr>
<td>Fracture risk incorrectly represented</td>
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</tbody>
</table>
1.2 Bone mineral measurements and diagnosis of osteoporosis

The objective findings that are provided by the measurement of bone mineral density deal with providing diagnostic criterion and establishing a prognostic value on the probability of occurring fractures in the future. BMD represents the amount of bone mass per unit volume, volumetric density, or per unit area, also known as areal density. [1]

It is reasonable and recommendable to clinically assess age and risk factors when deciding which women to screen. [17]

The technique of BMD implies X-ray absorptiometry (DXA), since the absorption of X-rays results in being very sensitive to the content of bone tissue, namely calcium. Dual-energy X-ray absorptiometry (DXA) is the most widely implied bone densitometric technique.

Several guidelines favor the simultaneous use of BMD at the proximal femur and lumbar spine in order to evaluate and assess the patient. The prediction of fractures is not improved by the use of multiple sites. Patients being selected on the basis of a minimum value of 2 or more tests will increase the number of patients selected and meeting the diagnostic criterion. [1]

Diagnostic thresholds

The diagnosis of osteoporosis is clinically and/ or radiographically. Osteoporosis may present with low-impact fractures (occurring from a fall at or below standing height) or with the occurrence of fragility fractures (occurring spontaneously). [17]
Four descriptive categories can be classified for adult men and women when using measurements of DXA at the femoral neck.

1) Normal value: Measurement value higher than 1 standard deviation below the reference mean of a young adult female. The T-score greater than or equal to -1 SD is considered normal.

2) Osteopenia (decreased bone mass): Measurement value with more than 1 standard deviation below the reference mean of a young adult female, but less than 2.5 SD. The T-score < -1 and > -2.5 SD.

3) Osteoporosis: Measurement value of 2.5 or more below the reference mean of a young adult female. The T-score less or equal to – 2.5 SD.

4) Severe Osteoporosis: Measurement value of 2.5 or more below the reference mean of a young adult female, plus the presence of one or more fractures related to fragility. [1]
1.3 “Official Positions of the ISCD (International Society for Clinical Densitometry) 2015” and the “Osteoporozės ambulatorinio gydymo kompensuojamaisiais vaistais tvarkos aprašas 2015 – Compensated ambulatory osteoporosis medical procedures 2015”

The International Society for Clinical Densitometry (ISCD) is considered a “not-for-profit multidisciplinary professional with the mission to advance excellence in the assessment of skeletal health.”

Several indications are being represented as the official positions of the ISCD. Bone Mineral Density (BMD) testing should be indicated in following conditions: [18]

1) Women aged 65 and older
2) For post-menopausal women younger than the age of 65, a bone density test is indicated if certain risk factors are present:
   - Decreased body weight
   - Previous fracture
   - Use of medication classified as high risk
   - Disease or medical condition which is associated with increased bone loss and deterioration
3) Women during the post-menopausal transition, where clinical risk factors, such as fracture, decreased body weight, previous fracture or the use of a high-risk medication are present
4) Men aged over 70 and older
5) Men being younger than 70; BMD is indicated if following risk factors are present:
   - Decreased body weight
   - Previous fracture
   - Use of medication classified as high risk
   - Disease or medical condition which is associated with increased bone loss and deterioration
6) Fragility fractures in adults
7) Diseases associated with low bone mass or bone loss
8) Medications associated with low bone mass or bone loss
9) Patients being considered for pharmacologic therapy
10) Monitoring of treatment effectiveness
11) Patients that are not receiving treatment and in which bone loss is evident, leading to initiation of therapy. [18]
Clinical risk factors according the “Osteoporožės ambulatorinio gydymo kompensuojamaisiais vaistais tvarkos aprašas 2015 – Compensated ambulatory osteoporosis medical procedures 2015” are as following:

1) Women aged 65 and older
2) Men aged over 70 and older
3) Female gender
4) Early menopause (younger than 45 years of age)
5) Rheumatoid arthritis
6) Low body mass index, < 19 kg/ m²
7) Other secondary causes of osteoporosis, diseases and conditions in addition to medicines that increase the risk of osteoporosis
8) Parents which suffered hip fractures
9) Previous osteoporotic fractures
10) Glucocorticoid treatment with over 5 mg of prednisone daily for at least 3 months
11) Alcohol consumption
12) Radiologically confirmed fractures (shoulder and upper arm, rib, femoral fracture, lumbar fracture, spine fracture [7]

The majority of osteoporotic fractures are due to the consequences of falls. It is important to evaluate these fall risk factors.

1) Age over 80
2) Report of falls in the last 12 months
3) Hearing impairment
4) Vision impairment
5) Intake of more than 4 drugs
6) Use of psychotropic drugs
7) Musculoskeletal diseases or conditions which disrupt balance or coordination [7]

When comparing the official positions of both guidelines, one on an international level and the other one on national level, representing Lithuania, it can be stated that no major differences are to be pointed out.
1.4 Distribution of osteoporosis and its properties

Osteoporosis represents a common health problem, having a progressive prevalence in both, the developed and developing countries.

According to the World Health Organization (WHO), osteoporosis is defined as a reduction in bone mineral density (BMD) of 2.5 standard deviations or more below that of the mean peak BMD of young adults when measured by dual-energy x-ray absorptiometry (DXA). [6]

Osteoporosis is influenced by different risk factors, being a multifactorial disease and having a complex pathophysiology, which could be caused by genetic, endocrine disorders and nutritional factors. Osteoporosis has a higher prevalence in women than men, 34% versus 17%. [8]

The consequences of osteoporosis in men and women are similar, such as increased fracture incidence, health care use, disability and resulting mortality. It is needless to say that the incidence of osteoporosis in female is higher than in case of male individuals, this being due to estrogen-deficient bone loss [9].

Majority of osteoporosis cases is present in postmenopausal women. However, vitamin D insufficiency and hyperparathyroidism represent the main causes of osteoporosis and premenopausal women. The worldwide incidence of osteoporosis is expected to rise by 240% in women and 310% in men by the year of 2050. [6]

The correlation assessment can be described as following:

1) 100% of selected patients were considered to undergo bone mineral density (BMD) measurement, of which 70% resulted in the diagnosis of osteoporosis and 30% in the diagnosis of osteopenia.

2) The weight distribution of the analyzed data represents 38% of the patients being underweight (<18,5 kg/m²), 28% of the patients represent a normal weight (18,5-24,9 kg/m²), 30% of the patients are overweight (25-29,9 kg/m²) and 4% of the patients are obese (>30 kg/m²).

In correlation, it can be stated that by analyzing the weight distribution of BMD measurement of the patients, underweight plays a significant role in the reason of indication.
1.4 Cancer and its effects on bone mineral density (BMD)

Breast cancer represents the most frequent malignant form of disease among women worldwide with an estimated 1.67 million new cases diagnosed in the year of 2012 (25% of all cancers in women) and being the fifth most common cause of death from cancer (522,000 deaths). [13]

According to the American Cancer Society there will be nearly 300000 new breast cancer cases diagnosed worldwide and approximately 50000 women will die from breast cancer in 2016. [14]

After all, survival of breast cancer has improved remarkably, which is likely to be explained by the use and earlier diagnosis via mammography screening. Advances in cancer-directed treatments also account for today’s success in combating breast cancer.

More than 80% of breast cancer patients are expected to live for 10 years or longer, it becomes increasingly more important to focus on the late-term effects induced by adjuvant treatment options, such as osteoporosis. [13]

Secondary causes of osteoporosis are disease states or medical conditions other than menopause and aging, which cause acceleration in bone loss. The prevalence of secondary bone loss and deterioration ranges from 30% to 50%. The use of standard chemotherapeutic agents in the treatment of breast cancer have implied an increase in the progression of bone loss through direct or indirect effects, however it is important to state that adjuvant therapy has mixed actions on bone. [15]
1.5 Accuracy of DXA measurement and importance of consideration of risk factors in patients

Low Bone Mineral Density (BMD) is a strong risk factor to be associated for future fractures and their occurrence. To complete a fracture risk assessment, a measurement of BMD is often included. The standard method for such a measurement is at the moment Dual energy X-ray Absorptiometry (DXA). The fracture risk increases approximately 1.5 to 2.6 fold for every decrease of one Standard Deviation (SD) in BMD from the age-standardized mean. DXA thus by is the recommended technique nowadays to establish the diagnosis of osteoporosis.

In most national and international guidelines and recommendations a DXA measurement of the hip (proximal femur) and lumbar spine is included as a part of fracture risk assessment. [24]

However it does not always give an evaluation of the patient's true bone quality and this should be considered. Fracture risk is composed of quality and quantity. The information about fracture risk obtained from a DXA is only ~20% of the patient's total risk.

Bone density results have to be evaluated and analyzed with caution, due to the fact that many factors can cause the results to be significantly, and often falsely, changed.

Reasons included are: artifacts, anatomy, machinery, location, varying technicians among others. [25]

DXA has been considered insufficient as a single predictor in a fracture risk assessment, for this reason several other methods for fracture prediction, alternative or supplemental to DXA, have been developed, such as FRAX. [24]

Women are at a greater risk of developing osteoporosis due to the rapid decline in estrogen levels during menopause. The decrease in estrogen levels cause bones to lose calcium and other minerals at a much faster rate, resulting in bone loss of approximately 2% per year occurring several years after menopause.

Men lose bone as they age as well, however testosterone levels in men decline more gradually and slower, resulting in bone mass remaining adequate till later in life.

Bone health is strongly inherited, consideration of family history of osteoporosis is important to consider and to note if anyone in the family (particularly parents or siblings) has ever been diagnosed with osteoporosis, experienced a bone fracture from a minor fall or has rapidly lost height. [25]
Important risk factors according the ISCD recommendations and guidelines:

1) Women aged 65 and older
2) Women during the post-menopausal transition, where clinical risk factors, such as fracture, decreased body weight, previous fracture or the use of a high-risk medication are present
3) Men aged over 70 and older are to be considered for BMD measurement.
4) Diseases associated with low bone mass or bone loss
5) Medications associated with low bone mass or bone loss
6) Use of glucocorticoids. [18]
1.6 Sarcopenia and fracture risk association in osteoporosis

A number of structural and functional changes are associated with aging which are conducive and beneficial to increased disability, frailty and falls. Factors contributing for the physical impairments are a gradual deterioration of bone (osteoporosis) and a progressive decline in muscle mass (sarcopenia).

Osteoporosis is characterized by low bone mass and micro-architectural deterioration of bone tissue and structure, leading to enhanced bone fragility and a consequent increase in fracture risk and fracture occurrence.

The European Working Group on Sarcopenia in Older People (EWGSOP) had already defined sarcopenia as a syndrome characteristic for progressive and generalized loss of skeletal muscle mass (SM) and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.

Musculoskeletal deterioration is an important and evident feature of frailty. An age-related decline in musculoskeletal health is documented, especially for bone, with more recent attention and focus directed towards the decline in skeletal muscle mass and function.

Associations between decreased bone mineral density (BMD), accelerated bone loss, fracture risk and mortality have been described.

Bone mineral density (BMD) is influenced several factors, such as ethnicity, geographic factors, diet, exercise, family history, and other lifestyle factors. [27, 29, 30]

General risk factors for osteoporosis include female sex, age, low body weight, chronic glucocorticoid use and certain endocrinopathies such as hyperthyroidism and primary hyperparathyroidism. A study on aging and body composition reveals the prevalence of sarcopenia were 8.9% in the overweight category (BMI = 25–29) group and 7.1% in the obese category (BMI >30) group. Overweight to obese but otherwise healthy people frequently do have sarcopenia as well.

A decrease in skeletal muscle, or also known as sarcopenia, has now been considered and discovered as a risk factor for osteoporosis. [31]

Importantly to stress and mention, sarcopenia is well known to be highly correlated with frailty, increased risk of falling and fracture risk association in the elderly.

In addition to increasing the risk of falling, sarcopenia might also decrease bone strength by reducing mechanical loading on the skeleton of affected individuals.
Sarcopenic individuals more often experience tiredness during daily activities and have lower fat mass, lean mass and weight in general. It is strongly associated to reduction of the global physical strength and mobility, ultimately the patient experiencing falls and fractures with an increased risk of mortality. [31]
RESEARCH METHODOLOGY AND METHODS

Statistical data analysis

The statistical data analysis has been performed by using the data collection and analysis system called SPSS 20.0 (Statistical Package for Social Science for Windows) package. The characteristics of chosen patients for this research are being described by using the concepts of general statistics, which imply location, dispersion, symmetry (minimum and maximum value, median value).

The normality of parametric distribution has been investigated by the Kolmogorov-Smirnov test. In case of normal parametrical distribution, the t-test was used for comparison of the quantitative size of two independent groups.

When more than two groups of a given set of normally distributed populations, all having the same standard deviation were examined, the „ANOVA“-method was used. In case of variables not meeting distribution normality, the significance was found by a non-parametric method, the so called „Mann-Whitney U test“. The difference will be considered as statistically significant when \( p < 0.05 \).

Methods:

A sample of 102 participants has been collected (\( M_{age} = 72.54, SD_{age} = 5.72 \), females 85.3%, males 14.7 %). All patients are of Lithuanian descent and were medically recorded as a result of receiving treatment as patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences. The DXA measurements which have been carried out in the year of 2016 in the Lithuanian University of Health Sciences were done according to the guidelines of the International Society for Clinical Densitometry (ISCD) in two skeletal sides of measurement: the lumbar spine and the proximal femur (neck and total hip).

The files have been obtained anonymously from the Endocrinology outpatient during the period of November 2016 - December 2016.

The data relevant for this research deals with following aspects:

Sociodemographic: Age, sex, weight, height, BMI

Reasons of DXA indication: Age, sex, weight, underweight, overweight, endocrine diseases which are responsible for causing secondary osteoporosis and breast cancer patients on current treatment with aromatase inhibitors (AI).
RESULTS

Results according to ISCD recommendations

In 100% of the researched individuals in which DXA measurement has been performed, the DXA performance has been done according to the International Society for Clinical Densitometry (ISCD) recommendations.

![Figure 1: Results of conducted BMD measurements according to ISCD recommendations in research individuals](image)

**Figure 1: Results of conducted BMD measurements according to ISCD recommendations in research individuals**

Figure 1 describes the results of conducted BMD measurements in 102 research individuals according to the ISCD recommendations and guidelines in research individuals. 70% of the patients who underwent a BMD measurement are affected by osteoporosis and 30% of the patients who underwent a BMD measurement are affected by osteopenia.
Figure 2: Age distribution according to ISCD recommendation and guidelines

Figure 2 describes the age distribution according to ISCD recommendation and guidelines. In the category “Men over 70”, 15 male patients have been evaluated. In the category “Women over 65”, 87 female patients have been evaluated.

According to the ISCD recommendations and guidelines 15 male patients and 87 female patients met the criterion regarding age as an indicative factor for BMD measurement.
Correlation between age, sex, weight, height, BMI and bone mineral density (BMD) measurement results

Figure 3: Research individuals grouped in age columns

Figure 3 describes the amount of research individuals subdivided age columns. 46 research subjects are from the age group of 65-70 years. 37 research subjects are from the age group 71-80 years, 18 research subjects are from the age group 81-90 years. 1 research subject is from the age group > 90 years.

According to the ISCD recommendations and guidelines the majority of patients are over 65 years of age and above and thus by meet the criterion regarding age as an indicative factor for BMD measurement.
Figure 4: Gender distribution for BMD measurements

Figure 4 describes the distribution of genders between male and female patients in which BMD measurements have been conducted. 15 male patients (14.7 %) and 87 total female patients (85.3 %), 15 of which are breast cancer patients on current aromatase inhibitor (AI) treatment, are used in the data distribution and collection of this research. Women make an amount of 85.3% of the total patient sample. According to the ISCD recommendations and guidelines female sex is an indicative factor for a BMD to be conducted. According to the ISCD recommendations and guidelines female patients represent the largest group in which BMD measurements have been conducted and thus by represent the criterion regarding female sex as an indicative factor for BMD measurement.
Figure 5: Conducted BMD measurements in women older than 65 years of age

Figure 5 describes the amount of conducted BMD measurement for female patients over the year of 65.

100% of the research individuals meet the criterion of the ISCD indications regarding BMD measurements.

According to the ISCD recommendations and guidelines female patients aged > 65 years of age represent the age and sex criterion as an indicative factor for BMD measurement.
Figure 6: Conducted BMD measurements in men older than 70 years of age

Figure 6 describes the amount of conducted BMD measurement for male patients over the year of 70.  
100% of the research individuals meet the criterion of the ISCD indications regarding BMD measurements. 
According to the ISCD recommendations and guidelines male patients aged > 70 years of age represent the age and sex criterion as an indicative factor for BMD measurement.
Figure 7 describes the mean T-score obtained through DXA measurement in three locations, namely the lumbar spine, hip neck and hip (proximal femur) of male patients aged older than 70 years of age. The mean T-score of spinal DXA measurement is -2.9 (SD -2.3). The mean T-score of the hip neck DXA measurement is -2.6 (SD -2) and the mean T-score of hip DXA measurement is -2.9 (SD -2.3). According to the ISCD recommendations and guidelines male patients aged > 70 years of age represent one criterion regarding an indicative factor for BMD measurement which has to take place in three locations, lumbar spine, hip neck and hip (proximal femur).
Figure 8 describes the mean T-score obtained through DXA measurement in three locations, namely the lumbar spine, hip neck and hip (proximal femur) of female patients aged older than 65 years of age. The mean T-score of spinal DXA measurement is -2.58 (SD -1.6). The mean T-score of the hip neck DXA measurement is -2.53 (SD -1.9) and the mean T-score of hip DXA measurement is -2.9 (SD -2.3).

According to the ISCD recommendations and guidelines female patients aged > 65 years of age represent one criterion regarding an indicative factor for BMD measurement which has to take place in three locations, lumbar spine, hip neck and hip (proximal femur).
Figure 9: BMI results of evaluated patients

Figure 9 describes the BMI results of the patients, which have received an indication to pursue BMD measurement. As depicted on the pie chart, 38% of the patients are underweight, the value being represented by $<18.5 \text{ kg/m}^2$. 28% of the patients represent a normal weight, the value being represented from 18.5-24.9 kg/m². 30% of the patients are overweight, the value being represented from 25-29.9 kg/m². 4% of the patients are obese, the value being represented by $>30 \text{ kg/m}^2$. According to the ISCD recommendations and guidelines underweight patients represent a criterion as an indicative factor for BMD measurement. 38% of patients meet the requirement. All 102 research individuals are included.
Figure 10: Prevalence of osteoporosis (column 1) and osteopenia (column 2) in underweight patients.

Figure 10 describes the prevalence of osteoporosis and osteopenia in underweight patients. Osteopenia is present in 8 underweight research subjects and osteoporosis is present in 30 underweight research subjects.
Results of the correlation between breast cancer patients on current treatment with aromatase inhibitors (AI) and the result of bone mineral density measurement

**Figure 11: Mean T-scores in performed DXA locations for breast cancer patients**

Figure 11 describes the mean T-score obtained through DXA measurement in three locations, namely the lumbar spine, hip neck and hip (proximal femur). The mean T-score of spinal DXA measurement is -3.9, (SD -2.8). The mean T-score of the hip neck DXA measurement is -3.4 (SD -2.9) and the mean T-score of hip DXA measurement is -2.9 (SD -2.4).

According to the ISCD recommendations and guidelines patients consuming medications associated with low bone mass or bone loss due to its pharmacologic effect (e.g. aromatase inhibitors) and patients being considered for pharmacologic therapy meet the criterion regarding indicative factors for BMD measurement which has to take place in three locations, lumbar spine, hip neck and hip (proximal femur).
Figure 12: Mean BMI and age values of breast cancer patients

Figure 12 describes the mean BMI and age values of breast cancer patients. The mean BMI value of breast cancer patients is 25.53 kg/m², representing a slight elevation and classifying as overweight. The age value of breast cancer patients is 67.8 years of age. According to the ISCD recommendations and guidelines female patients aged > 65 years of age represent one criterion regarding an indicative factor for BMD measurement which has to take place in three locations, lumbar spine, hip neck and hip (proximal femur).
BMD measurement results in patients aged > 65 years in the category of normal weight patients and underweight patients and relate it to sarcopenia

Figure 13: Mean T-scores in performed DXA locations for patients aged > 65 years of age and normal weight.

Figure 13 describes the mean T-score obtained through DXA measurement in three locations, namely the lumbar spine, hip neck and hip (proximal femur) for patients aged older than 65 years of age and of normal weight. The mean T-score of spinal DXA measurement is -2,2 (SD -1,4). The mean T-score of the hip neck DXA measurement is -2,15 (SD 1,3) and the mean T-score of hip DXA measurement is -3,05 (SD -2,4).
Figure 14: Mean T-scores in performed DXA locations for patients aged > 65 years of age and underweight.

Figure 14 describes the mean T-score obtained through DXA measurement in three locations, namely the lumbar spine, hip neck and hip (proximal femur) for patients aged older than 65 years of age and being underweight. The mean T-score of spinal DXA measurement is -2.7 (SD -1.6). The mean T-score of the hip neck DXA measurement is -2.5 (SD -1.5) and the mean T-score of hip DXA measurement is -2.6 (SD -1.5).

Result number 15
Metabolic bone diseases more frequently affect women than men. This has been proven with the help of “Mann-Whitney U test”. The p-value is 0.0394. The result is significant at p < 0.05.

Result number 16
Underweight patients suffering from osteoporosis disclose a significant T-score alteration. This has been proven with the help of “Mann-Whitney U test”. The p-value is 0.0351. The result is significant at p < 0.05.
DISCUSSION

In this research, a sample of 102 participants has been collected (\(M_{age} = 72.54, \ SD_{age} = 5.72, 85.3\%\), of which are females and 14.7\% of which are males). All patients are of Lithuanian descent and were medically recorded as a result of receiving medical attention as patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences. The main aim of this thesis was to evaluate and disclose the indications that led to the measurement of bone mineral density among patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences in the context of the guidelines and recommendations of the International Society for Clinical Densitometry (ISCD).

In 100\% of the researched individuals in which DXA measurement has been performed, the DXA performance has been done according to the International Society for Clinical Densitometry (ISCD) recommendations. 30\% of performed measurements were compatible with osteopenia and 70\% of performed measurements were compatible with osteoporosis.

In the category “Men over 70”, 15 male patients have been evaluated. In the category “Women over 65”, 87 female patients have been evaluated.

According to the ISCD recommendations and guidelines, age (men > 70 years of age, women > 65 years of age) and female sex are indicative for the performance of bone mineral density (BMD) measurement. [18]

15 male patients (14.7 \%) and 87 total female patients (85.3 \%), 15 of which are breast cancer patients on current aromatase inhibitor (AI) treatment, are used in the data distribution and collection of this research and represent research individuals.

The majority of patients are of female sex, undermining the importance of sex being a strict and important indicator for bone mineral density (BMD) measurements to be performed.

This specific distribution and result is also reinforced by international and national guidelines and recommendations, which are applied in Lithuania. [7, 18]

38\% of the research individuals are underweight, the value being represented by <18.5 kg/m\(^2\). When taking a closer look, underweight does represent an indicative factor for a bone mineral density (BMD) measurement to be performed, interestingly enough it can also be associated with decreased muscle mass, also known as sarcopenia. Underweight implies a high-risk factor in the development and diagnosis of metabolic bones diseases and should always be considered when assessing a patient.
Musculoskeletal deterioration is a crucial and evident feature of frailty. An age-related decline in musculoskeletal health is documented, especially for bone, with more recent attention and focus directed towards the decline in skeletal muscle mass and function. Associations between decreased bone mineral density (BMD), accelerated bone loss, fracture risk and mortality have been described. [18,27, 29]

Breast cancer patients have been evaluated comparing the mean T-scores, resulting that among the selected breast cancer patients on current aromatase inhibitors (AI) depict the highest T-score in the lumbar spine.

More than 80% of breast cancer patients are expected to live for 10 years or longer, it becomes increasingly more important to focus on the late-term effects induced by adjuvant treatment options, such as osteoporosis, including future fractures. [13]

The mean value of age is 67.8 years of age and a BMI of 25.53 kg/m², representing most of the patients being > 65 years of age, which is according to the ISCD recommendations and guidelines, age an indicative factor for the performance of bone mineral density (BMD) measurement. [18]

Weight wise overweight is present in the research subjects of breast cancer patients.

The mean T-score obtained through DXA measurement in two locations, namely the lumbar spine and proximal femur (hip neck and hip) for patients aged older than 65 years of age and being underweight is -2.7 in spinal DXA measurement is. The mean T-score of the hip neck DXA measurement is -2.5 and the mean T-score of hip DXA measurement is -2.6. As previously mentioned, underweight does represent an indicative factor according to the recommendations and guidelines of the ISCD. Associations between decreased bone mineral density (BMD), accelerated bone loss, fracture risk, mortality and underweight have been described. [18,27, 29]

Importantly to be mentioned and to be highly stressed is the analysis and identification of risk factors, even then, when a diagnosis of metabolic bone diseases has not even been confirmed or reaffirmed. Risk factor analysis and taking a proper and detailed anamnesis of the patient’s current state in all fields is to be highly disclosed and approached.

In statistics, the Mann–Whitney U test is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be less than or greater than a randomly selected value from a second sample. With the help of this test it has been proven that metabolic bone diseases more frequently affect women than men. The p-value is 0.0394. The result is significant at p < 0.05.
CONCLUSIONS

Conclusion:

1. All the conducted BMD measurements by DXA (indications, technologist’s positioning and radiological analysis) among patients of the Endocrinology outpatient department of the Lithuanian University of Health Sciences have been performed according to the International Society for Clinical Densitometry (ISCD) recommendations.

2. Osteopenia was determined in 30% of research individuals and osteoporosis was determined in 70% of research individuals (15 male patients > 70 years of age and 87 female patients).

3. 38% of research individuals are underweight (BMI <18,5 kg/m²).

4. Breast cancer patients on current aromatase inhibitor (AI) treatment meet the age, sex and pharmacologic therapy criterion regarding the International Society for Clinical Densitometry (ISCD), the mean age being 67.8 years of age; the weight criterion is not fulfilled, thus by research individuals being of overweight BMI classification and representing a T-score of -3.9 in the lumbar spine BMD measurement. Fracture risk is increased in this anatomical location.

5. Underweight in addition to suspicion of sarcopenia does represent a significantly high risk factor in fracture and falling risk.
PRACTICAL RECOMMENDATIONS

Recommendations:

1. BMD measurements are necessary to be done according to the ISCD recommendations.
2. BMD measurements are necessary to be conducted in elderly individuals who suffer from underweight and where sarcopenia is suspected.
3. BMD measurement should be performed in 2 skeletal sides, namely the lumbar spine and proximal femur.
4. Fall prevention and taking preventive measures including fall avoidance and risk factor avoidance should be strictly applied, thus by decreasing future fractures; preventive measures are to be taken and recommended without diagnosis of osteoporosis.
5. Assessment of risk of falls and their prevention, including maintenance of mobility and correction of nutritional deficiencies, particularly of calcium, vitamin D and protein, should be advised and are to be strictly encouraged.
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