REVISTA CIÊNCIAS e ODONTOLOGIA

RADIOMORPHOMETRIC INDICES FOR MEASUREMENT OF MINERAL AND BONE DISORDERS IN CHRONIC KIDNEY DISEASE: A LITERATURE REVIEW

ÍNDICES RADIOMORFOMÉTRICOS PARA MEDIÇÃO DAS DESORDENS MINERAL E ÓSSEA NA DOENÇA RENAL CRÔNICA: UMA REVISÃO DE LITERATURA

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Abstract

Introduction: the functional deficiency of the kidneys compromises the homeostasis of calcium, phosphorus, vitamin D and parathyroid hormone (PTH), promoting a condition called mineral and bone disorder of chronic kidney disease (BMD-CKD). Radiomorphometric indices such as mandibular cortical index, panoramic mandibular index, mental index, antegonial index, gonial index and trabecular bone pattern were developed to evaluate bone structure. **Aim:** the objective of the study was to correlate CKD-BMD with radiomorphometric indices, through a literature review. **Methods:** it was carried out a search in the National Library of Medicine (PubMed) database, using the terms: chronic kidney disease, chronic kidney insufficiency, panoramic radiography, cone-beam computed tomography and radiomorphometric indices, from 2013 to 2024. The articles were selected according to the objective of the proposed review. **Results:** data from 12 clinical studies that evaluated the correlation between CKD–MBD and radiomorphometric indices. **Discussion:** according to the studies found, radiomorphometric indices detected bone changes in the mandible and were correlated with secondary hyperparathyroidism due to increased PTH, with increased action of osteoclasts on the bone and release of skeletal calcium, soon resulting in progressive bone loss. **Conclusions:** radiomorphometric indices can contribute to screening for the detection of bone changes in patients with CKD and clinicians must be vigilant for bony changes on dentomaxillofacial imaging in these patients with CKD.

Keywords: chronic kidney disease-mineral and bone disorder; panoramic radiography; cone-beam computed tomography.

Resumo

Introdução: a deficiência funcional dos rins compromete a homeostase do cálcio, fósforo, vitamina D e do paratormônio (PTH) promovendo um quadro denominado distúrbio mineral e ósseo na doença renal crônica (DMO-DRC). Os índices radiomorfométricos como o índice cortical mandibular, índice mandibular panorâmico, índice mentoniano, índice antegoníaco, índice goníaco e padrão do osso trabecular foram desenvolvidos para avaliar a estrutura óssea. **Objetivo:** objetivo do estudo foi correlacionar o DMO-DRC com os índices radiomorfométricos, por meio da revisão de literatura. **Métodos:** foi realizada uma busca na base de dados *National Library of Medicine (PubMed)*, utilizando os termos: doença renal crônica, insuficiência renal crônica, radiografia panorâmica, tomografia computadorizada de feixe cônico e índices radiomorfométricos, de 2013 a 2024. Os artigos foram selecionados de acordo com o objetivo da revisão proposta. Resultados: dados de 12 estudos clínicos que avaliaram a correlação entre DMO-DRC e índices radiomorfométricos. **Discussão:** de acordo com os estudos encontrados, os índices radiomorfométricos detectaram as alterações ósseas na mandíbula e estavam correlacionados com o hiperparatireiodismo secundário devido ao aumento do PTH, com o aumento da ação dos osteoclastos no osso e liberação do cálcio esquelético, logo resultando na perda óssea progressiva. **Conclusões:** os índices radiomorfométricos podem contribuir na triagem na detecção das alterações ósseas nos pacientes com DRC e os clínicos devem estar atentos às alterações ósseas nas imagens dentomaxilofaciais nesses pacientes com DRC.

Palavras-chave: distúrbio mineral e ósseo na doença renal crônica; radiografia panorâmica; tomografia computadorizada de feixe cônico.

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Introduction

Chronic kidney disease (CKD) is a global problem, with an increasing prevalence and burden on health care.[1] Although diabetes and hypertension are the most common causes of CKD, other etiologies can lead to progressive loss of kidney function.[2] CKD is defined as functional and structural alterations lasting >3 months, a glomerular filtration rate (GFR) <60 mL/min/1.73 m^2, and presence of markers of kidney damage, such as albuminuria and hematuria. CKD is divided into five stages; in stage 5, known as end-stage renal disease,[3] the GFR is <15 mL/min/1.73 m^2.

Functional impairment of the kidneys compromises the homeostasis of calcium, phosphorus, vitamin D, and parathormone (PTH). This leads to a set of skeletal alterations known as mineral and bone disorder (MBD) in CKD (CKD–MBD),[4] including a decrease in the serum level of active vitamin D3, which decreases calcium retention by the renal tubules and reduces calcium absorption in the gastrointestinal tract. Calcium elimination through the urine increases, resulting in hypocalcemia which leads to secondary hyperparathyroidism. The consequent increase in osteoclasts in the bone and fibroblast growth factor 23 levels results in calcium removal from the bones, leading to hypercalcemia.[5]

CKD–MBD can affect the craniofacial bones. Among the dentomaxillofacial manifestations of CKD–MBD are changes in the trabecular pattern of the bone, soft-tissue calcifications, loss of the lamina dura, pulp calcification, and bone loss due to periodontal disease.[6-7] Renal osteodystrophy refers to the bone pathologies observed in patients with CKD. The pathologies vary according to exogenous (e.g. medication, type of dialysis) and endogenous (e.g. age, sex) factors. Therefore, clinical examination and laboratory and imaging tests are used for the diagnosis of renal osteodystrophy.[8]

This study aimed to evaluate the correlation between CKD–MBD and radiomorphometric indices using imaging tests used in dentomaxillofacial diagnosis, based on a literature review.

Methods

The articles were searched in the following database: National Library of Medicine (PubMed), during the month of July 2024. In the study, all types of English-language published articles were evaluated and included. Only clinical studies were selected for literature review.

The articles corresponding to the period from 2013 to 2024 were included. The following keywords were used as search descriptors: chronic kidney disease, chronic kidney insufficiency, panoramic radiography, cone-beam computed tomography and radiomorphometric indices. The articles were selected according to the objective of the proposed literature review.

Results

Initially, 129 studies were found through a search in the National Library of Medicine (PubMed). All studies had their titles and abstracts evaluated following the inclusion and exclusion criteria. About 97 studies were excluded after reading the titles and abstracts. In the screening process, 20 duplicate articles were excluded. After that analyse,12 articles were included in this literature review

Clinical studies that evaluated the correlation between mineral and bone disorder in chronic kidney disease and radiomorphometric indices. The article selection flowchart was represented in Figure 1. The Table 1 presented the tabulation of results, containing the authors, year of publication, objective, methodology and results of each article included in the literature review.

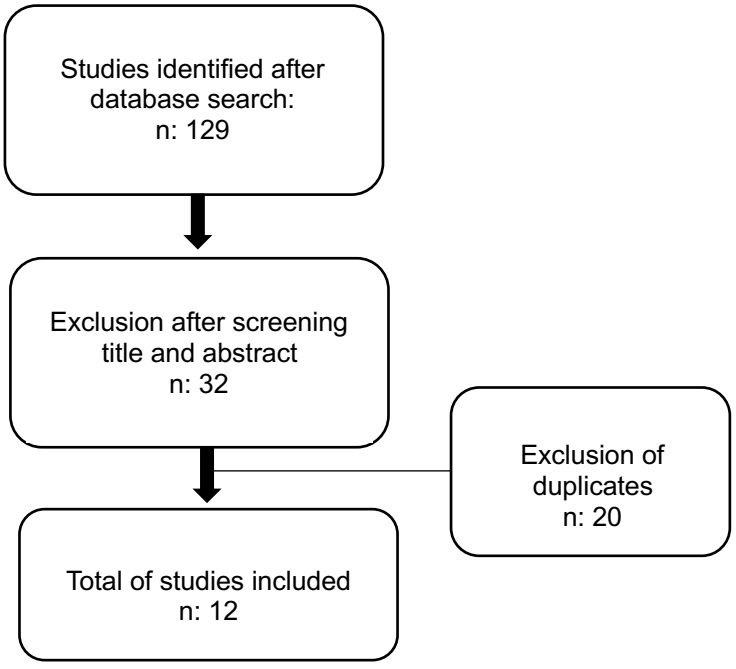

Figure 1 - Article identification and selection flowchart. Source: Authors.

Table 1. Data from clinical studies evaluating the correlation between CKD–MBD and radiomorphometric indices.

Authors/Year	Objective	Methodology	Results
Henriques et al., (2013)	The study investigated the association between osteoporosis progression (hands and jaw) and PTH levels.	30 patients in hemodialysis, stage 5 CKD, with serum PTH levels≥500 pg/ml, male patients and 45 years Four panoramic radiographic parameters (mental index, mandibular cortical index, trabecular bone pattern, and calcification/resorption) Four hand/wrist radiographic parameters (metacarpal cortical thickness, phalangeal cortical index, trabecular bone pattern, and calcification/resorption).	Mandibular cortical index was strongly correlated with the phalangeal cortical index. Phalangeal cortical index and trabecular bone pattern of hand/wrist correlated with PTH levels. Brown tumors occurred in four CKD patients, while both vascular calcifications and acroosteolysis were observed in 19 patients.
Henriques et al., (2014)	The study evaluated the effects of renal osteodystrophy using panoramic radiography parameters. The correlation between these parameters and parathyroid hormone (PTH) levels.	30 patients in hemodialysis, stage 5 CKD, with serum PTH levels≥500 pg/ml, male patients and 45 years 60 controls Qualitative paramenters (mandibular cortical index/ trabecular bone pattern) Quantitative parameters (mental index/calcification and resorption foci).	Qualitative and quantitative parameters demonstrate significant difference compared with the control group and PTH levels were correlated with mental index, mandibular cortical index and trabecular bone pattern.
Massahud et al., (2018)	The study evaluated the effects of renal osteodystrophy in patients with mineral disturbance and bone loss, using panoramic radiography parameters and digital radiographs of the phalanges.	24 patients with CKD, 12 with PTH levels ≥500 pg/ml, and 12 with PTH levels <500 pg/ml. The mandibular cortical index (MCI) and the trabecular bone pattern index (TBP) The phalangeal cortical index (PCI).	Significant correlations were found between the PTH levels and the MCI, the PCI and the TBP index.
Abdinian et al., (2019)	The study investigated the bone changes of CKD stages 3–5 patients using digital panoramic radiography.	30 patients with CKD stages 3–5 and 30 controls Quantitative parameters: mental index (MI), panoramic mandibular index (PMI) and antegonial index (AI) Qualitative parameters: mandibular cortical index (MCI) and trabecular bone pattern (TP).	MCI and TP were significantly different between the two groups.

Queiroz et al., (2019)	The aim was to correlate radiomorphometric indices as an auxiliary method in bone evaluation in male and female patients with CKD-MBD and controls.	66 patients with CKD-MBD (38 men and 28 women) in stage 5 132 controls Mental index (MI), height at the mental foramen, total mandibular height (THM), panoramic mandibular index (PMI), original height of the mandible, alveolar bone resorption, distance from the mental foramen to the alveolar bone crest (MF-ABC), mandibular cortical index (MCI), trabecular bone pattern.	In female patients with CKD-MBD, moderate negative and significant correlations were observed between MI/PMI and PTH.
Järvisalo et al., (2021)	This study aimed the association between Panoramic Tomographic Index (PTI), and cardiovascular and all-cause mortality, major adverse cardiovascular events (MACEs), episodes of bacteremia and laboratory measurements during a three-year prospective follow-up in CKD stage 4–5 patients.	190 CKD stage 4–5 patients attended panoramic dental radiographs in the beginning of the study. The patients were followed up for three years or until death. MACEs, episodes of bacteremia, C-reactive protein and leukocytes were recorded during follow-up.	Radiographically assessed dental health was independently associated with all-cause and cardiovascular mortality and MACEs.
Abdinian et al., (2021)	The aim was to compare dental and skeletal indices in panoramic radiography between patients undergoing haemodialysis, peritoneal dialysis and control group.	Panoramic images of 32 haemodialysis patients, 14 patients under peritoneal dialysis and 52 healthy individuals were evaluated. Quantitative Indices: antegonial index (AI), mental index (MI) and panoramic mandibular index (PMI). Qualitative indices: mandibular cortical index (MCI) and trabecular pattern (TP).	AI, MCI and TP were significantly different between the two case groups and the control group.
Ostovarrad et al., (2022)	This study aimed to investigate the relationship between serum levels of PTH and dental and bone changes in the panoramic view of hemodialysis patients.	34 patients with CKD - PTH levels ≥300 pg/ml (case) 34 patients with CKD - PTH levels between 150 to 300 pg/mL (control) DMFT (decayed, missing and filled teeth) index, bone resorption, periodontal ligament, lamina dura, mandibular cortical thickness, bone granular pattern, pulp and periapical lesion and brown tumor.	Mandibular cortical thickness and bone granular pattern were significantly different between the two groups.

Moest et al., (2023)	The observational radiological case control study evaluated the impact of secondary hyperparathyroidism (SHPT) due to chronic kidney disease (CKD).	41 patients in hemodialysis, stage 5 CKD with pathologic PTH levels of 65 > pg/ml and with SHPT 41 controls Panoramic radiograph: mandibular cortical index (MCI), trabecular bone pattern (TBP), and calcification and resorption foci.	Statistically significant differences in the MCI and in the TBP between the groups The PTH level was significantly correlated with TBP.
Çağlayan et al., (2015)	The study evaluated the mandibular cortical indices (MCI), mandibular canal diameter, pulp chamber size, pulp calcification, lamina dura loss and soft-tissue calcifications in patients with chronic renal failure (CRF) and in healthy controls.	15 patients with CRF 15 healthy controls CBCT images: antegonial index (AI), mental index (MI), panoramic mandibular index (PMI), mandibular cortical index (MCI), pulp chamber size, number of teeth with pulp calcification and lamina dura loss.	There were no statistically significant differences in the PMI, MI and AI, pulp chamber size and pulp calcifications There were statistically significant differences in the MCI, soft-tissue calcifications and lamina dura loss.
Mohamed et al., (2021)	The study was undertaken to assess mandibular osseous changes using radiomorphometric indices by CBCT in patients with ESRF (end-stage renal failure) versus healthy population.	13 ESRF patients 13 controls CBCT images: mandibular cortical index (MCI), panoramic mandibular index (PMI), mental index (MI), gonial index (GI), and antegonial index (AI).	There was no significant difference between radiomorphometric indices of patients with ESRF and the control group.
Ersu et al., (2023)	The study evaluated the mandibular bone structure of patients with chronic renal failure (CRF) and compare to control group via radiomorphometric indices in the cone beam computed tomography (CBCT) images.	44 patients with CRF 44 controls CBCT images: CT cortical index (CTCI), CT mental index (CTMI), CT mandibular index (CTI).	There was no significant difference between radiomorphometric indices of patients with CRF and the control group.

Discussion

In patients with CKD with high PTH levels, skeletal catabolism progresses leading to the risk of pathological fractures and vascular and soft-tissue calcification owing to hypercalcemia.[9] Patients with CKD have a higher risk of hospitalization and a significantly higher risk of mortality owing to cardiovascular diseases; cardiovascular risk factors such as diabetes, smoking, hyperlipidemia, and hypertension; and skeletal catabolism.[10]

Alterations caused by hyperparathyroidism in patients with CKD are detected in imaging modalities used for dentomaxillofacial diagnosis, and they are particularly evident in the mandible.[11] Signs of mandibular bone alteration in CKD include cortical resorption, loss of the lamina dura, decrease in bone trabeculae (ground-glass appearance), presence of brown tumors, periodontal alterations, and vascular and soft-tissue calcifications.[12]

Radiomorphometric indices are used to assess bone loss on panoramic radiographs in patients with altered bone metabolism,[13] and cone-beam computed tomography (CBCT) can be used for bone assessment using radiomorphometric indices based on cortical bone measurements and trabecular bone characteristics.[14-15] Dental professionals can identify changes which are distinguished using radiomorphometric indices, such as the mandibular cortical, panoramic mandibular, mentonian, antegonial, and gonial indices, and the trabecular bone pattern, on imaging modalities. These indices have been developed to assess mandibular bone structure and detect bony changes in pathologies that cause structural changes in the bone, including MBD.[16]

Patients with CKD and high PTH levels have a higher frequency of bone alterations on panoramic radiographs and CBCT scans.[11-12] In patients with CKD, hypercalcemia due to high PTH levels is associated with an unfavorable prognosis[1-2] and indicates progression of CKD-MBD.[3] Therefore, imaging modalities such as panoramic radiography are important for detecting bony and dental alterations in patients with CKD-MBD.

Radiomorphometric indices measured on panoramic radiographs and CBCT are screening tools for osteoporosis and osteopenia.[13-14] A previous study reported a significant positive correlation between the mandibular cortical index assessed using panoramic radiographs and the cortical index of the phalanx in patients with CKD with a PTH level >500 pg/mL.[17] These data corroborate the findings in a case-control study,[18] that the mandibular cortical index, trabecular bone pattern, number of calcifications and resorptions, and mental index are significantly different between the groups. Patients with CKD and high PTH had moderate-to-severe cortical-bone erosion, sparse trabecular bone with a ground-glass appearance, a greater number of resorption and calcification sites, and a lower mental index.

The progressive stage of CKD associated with a high PTH level influences the imbalance in bone metabolism.[5] In a previous study, PTH levels were significantly correlated with the mandibular cortical index, trabecular bone pattern and phalangeal cortical index; patients with CKD with PTH level >500 pg/mL had more severe bony changes compared to patients with CKD with PTH level <500 pg/mL.[19] Other studies[20-21] reported that patients with CKD stages 3-5 and high PTH levels had a more eroded mandibular cortex, a more porous trabecular bone pattern and a lower mental index than controls.

Patients with CKD usually have diabetes mellitus and hypertension associated with other factors to determine cause and effect in the pathology, such as high PTH levels, prolonged dialysis and more advanced stages.[7] In a follow-up study of patients with CKD, the panoramic tomographic index was associated with all-cause mortality, coronary artery disease, and major adverse cardiovascular events; this association remained significant with the inclusion of age, referral to the dentist, diabetes, treatment modality, death, and end of follow-up.[22] Another study reported that patients with CKD undergoing hemodialysis had a lower antegonial index, greater porosity indicated by the mandibular cortical index, and a more porous trabecular bone pattern compared to patients with CKD undergoing peritoneal dialysis and controls.[23]

Disturbances in serum calcium, phosphate, PTH, and vitamin D levels affect bone remodeling and mineralization. Therefore, in patients with CKD, screening and monitoring are essential for accurate diagnosis and to reduce the disease burden.[10] In a previous study, patients with CKD with PTH levels >300 pg/mL demonstrated a more sparse trabecular bone pattern and reduced

thickness of the mandibular inferior cortex compared to patients with CKD with PTH levels between 150 to 300 pg/mL.[24] Another study reported that patients with CKD undergoing hemodialysis had a more porous trabecular bone pattern and greater porosity indicated by the mandibular cortical index compared to controls; however, no correlation between the significant increase in cortical erosion and higher PTH levels was observed, and the foci of resorption and calcification were not significantly different between the groups. Nonetheless, the trabecular bone pattern was affected by pathological PTH levels.[25]

CBCT has been used to determine radiomorphometric indices in various studies.[14-15] In a case-control study using CBCT, the mandibular cortical index revealed a more porous texture in patients with CKD, and the number of teeth with loss of lamina dura and soft-tissue calcifications were significantly greater in the patient group.[26] In another study using CBCT, bone quality in patients with CKD assessed using radiomorphometric indices was not significantly different than that in healthy patients.[27] These data corroborate the findings in another CBCT study which revealed no significant difference in the mental, mandibular cortical, and mandibular indices between the case and control groups.[28]

Analysis of studies that used radiomorphometric indices in patients with low bone mineral density revealed that the mental, mandibular cortical, and panoramic mandibular indices were used more frequently. However, compared with the standard dual-energy X-ray absorptiometry test, these indices have limitations such as the lack of standardization. Thus, further studies are needed for standardization. However, radiomorphometric indices correlated with clinical and laboratory findings are useful as screening tools for patients with MBD.[29] Integration of these tools with imaging modalities allows correlation of the imaging findings for the detection of alterations in bone metabolism in patients with MBD.[30]

Conclusions

Patients with CKD-MBD have a higher frequency of bony and dental alterations. *In* patients with CKD, radiomorphometric indices are correlated with elevated PTH levels. Clinicians must be vigilant for bony changes on dentomaxillofacial imaging in these patients. Considering that the diagnosis, prognosis, and treatment of patients with CKD involves a multi-disciplinary team, knowledge of this process is important for dental professionals.

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