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Correlation between skin and bone parameters in women with postmenopausal osteoporosis: a systematic review

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- Skin and bone share similarities in terms of biochemical composition.
- Some authors have hypothesized that their properties could evolve concomitantly with age, allowing the estimation of the parameters of one from those of the other.
- We performed a systematic review of studies reporting the correlation between skin and bone parameters in women with postmenopausal osteoporosis.
- Fourteen studies – including 1974 patients – were included in the review.
- Three of these studies included two groups of participants – osteoporotic and non-osteoporotic – in order to compare skin parameters between them: two studies found a significant difference between the two groups and one did not.
- Eleven of these studies included one population of interest and compared its skin and bone parameters in a continuous manner: eight studies compared dermal thickness to bone mineral density (seven found a significant correlation [$R = 0.19–0.486$] and one did not); two studies compared skin elasticity to bone mineral density (both found a significant correlation [$R = 0.44–0.57$); and one study compared skin collagen to bone mineral density and found a significant correlation ($R = 0.587$).
- It can be assumed that the estimation of skin alterations from ageing could help in estimating concomitant bone alterations.

Keywords: osteoporosis; menopause; ageing; skin; bone mineral density; epidemiology

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Introduction

Osteoporosis is a systemic condition associating a reduction of bone mass and a modification of bone micro-architecture. It leads to a mechanical fragility and a higher risk of fracture.[1] The exact pathophysiology of osteoporosis is still to be elucidated.[2] A decrease of osteoblastic activity with age and with the menopause seems related. However, biotypes – female, fair-skinned and slim – and environmental conditions are also implicated.[3] Because of important direct costs to the healthcare system and important indirect costs to government and to society, early detection of osteoporosis is a priority for public health.[4,5]

Both skin and bone tissues are mainly composed of collagen. Indeed, the dermis organic matrix comprises about 80% collagen and primarily type I collagen.[6] Moreover, the bone organic matrix comprises about 90% collagen and primarily type I collagen also.[7] This organic part of the bone has the special property of being covered by a mineral component that improves strength and hardens the framework. This specific association explains the capacity of the bone to resist mechanical stresses. Because the organic matrix of bone and skin shares these similarities, biochemical connections between skin and bone tissues could exist.

In 1963, McConkey et al reported that elderly women with osteoporotic fractures had a higher incidence of thin skin.[8] Later, Black et al confirmed the simultaneous occurrence of these events by reporting a correlation between transparent skin and osteoporosis.[9] These observations led to a hypothesis that skin thinning and bone loss could be correlated.[10] Recent investigations suggest that the processes involved in chronological atrophy of both tissues may overlap, thereby providing a foundation for further investigations.[11]

Given the importance of an early diagnosis of osteoporosis, the development of a probabilistic model to identify the persons at most risk in a certain population would have a great interest. In fact, current probabilistic models used to estimate the risk of osteoporotic fractures, such as the Fracture Risk Assessment Tool (FRAX), are mostly tools to identify a certain population with a higher risk of fracture. This population classically represents frail, old, white women, with a low bone mineral density (BMD), and a family history of femoral neck fracture. However, we lack a clinical tool that would allow us to go further in the estimation of the risk of fracture for a specific individual. Using the skin, we could be able to estimate the physiology of the specific individual, and then present to her/him a more personalized risk of fracture. Hence, measurement of skin parameters could be performed in order to fulfil that purpose. To test that hypothesis, we performed a systematic review of every study reporting relationships between skin and bone parameters in women with postmenopausal osteoporosis.

Our purpose was to answer the following questions: (1) what type of bone and skin parameters were compared in each study; (2) what was the importance of the relationship found between the bone and skin properties tested?

Methods

Protocol and registration

We specified in advance the objectives, methods of analysis and inclusion/exclusion criteria for this study. Subsequently, we documented them in a protocol. This protocol was registered and made publicly available at https://www.crd.york.ac.uk/prospero under the registration number CRD42014007351. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used in the design and conduction of the present systematic review.[12,13]

Eligibility criteria

Types of studies. We aimed to include studies comparing skin and bone parameters in women with postmenopausal osteoporosis. We considered only prospective trials, published in English or in French, without any restriction on publication date, given the fact that we anticipated no change in the relationship tested with the date of publication. We did not include any abstracts or unpublished material.

Types of participants. We included studies that considered women with postmenopausal osteoporosis only. Every study considering other conditions – such as steroid-related osteoporosis, anorexia nervosa, osteogenesis imperfecta – was excluded.

Types of intervention. We made no restriction on the type of intervention used to test skin properties – such as thickness measures, vacuum devices or echographs – or on the type of intervention used to test bone properties – such as radiographs or BMD.

Types of outcome measures. The primary outcome measure was the identification of the type of bone and skin parameters that were compared in each study. The secondary outcome measure was the importance of the relationship found between the bone and skin properties tested.

Information sources

We identified the studies by searching MEDLINE via PubMed, EMBASE and the Cochrane library. We ran the last search on 1 January 2016. The closing date was to be extended in case the retrieval period demanded a significant amount of time so that there would be little risk of excluding relevant and recent studies. We did not attempt to acquire any missing information (e.g. on study methods or results) from investigators or sponsors.

Search

We used the following search terms to search the aforementioned databases: skin and osteoporosis. For example, the search strategy for MEDLINE via PubMed was: ("skin"[MeSH Terms] OR "skin"[All Fields]) AND ("osteoporosis, postmenopausal"[MeSH Terms] OR ("osteoporosis"[All Fields] AND "postmenopausal"[All Fields]) OR "postmenopausal osteoporosis"[All Fields] OR "osteoporosis"[All Fields] OR "osteoporosis"[MeSH Terms]).

Study selection

Two authors (JCA and TB) performed the eligibility assessment independently in a non-blinded standardized manner. First, they reviewed the titles and abstracts resulting from the search. Then, all the studies selected were retrieved and evaluated further from the text to assess the inclusion and exclusion criteria. Finally, the two authors manually searched the references of every included study in order to detect any additional studies meeting the inclusion and exclusion criteria. Any disagreements between reviewers were resolved by consensus. In case a disagreement persisted, a third review by another author (TH) was performed.

Data collection process

We developed a data extraction sheet based on the Cochrane Consumers and Communication Review Group's data extraction template, pilot-tested it on the first five included studies, and refined it accordingly. Two authors (JCA and TB) extracted the data from included studies. The authors aimed to avoid the inclusion of

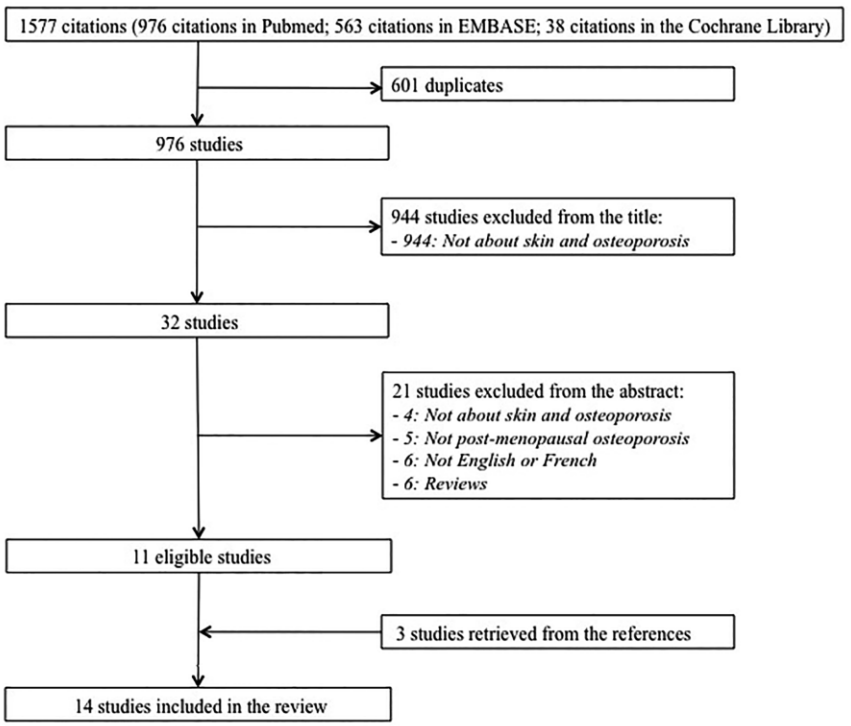

Fig. 1 Selection of the included studies.

multiple reports of the same study by juxtaposing author names, location of the study and sample sizes. When a duplicated study was suspected, only the more recent study was included. The previous reports were then used to complete any lack of data in the selected study. Disagreements were resolved by discussion between the two review authors; if no agreement could be reached, it was planned that a third author (TH) would decide. Finally, we did not contact any author to obtain further information from the included studies.

Data items

Information was extracted from each included trial on: (1) characteristics of trial participants (including date of inclusion, gender, age and conditions) and the trial's inclusion and exclusion criteria; (2) types of intervention (including types of skin parameter and types of bone parameter); (3) type of outcome measure (relationship found between the parameters). No new variable was added after the final review started.

Summary measures

The primary outcome measure was the identification of the type of bone and skin parameters that were compared in each study. This outcome was presented in a descriptive manner. The secondary outcome measure was the importance of the relationship found between the bone and skin parameters tested. When eligible, it was presented as a coefficient of correlation (*R*) between the skin and bone parameters.

Synthesis of results

Given the important heterogeneity expected between the parameters used, we anticipated a low consistency of results across the included trials. We decided to present the results as retrieved. Two types of presentation were performed: first, a presentation of the different studies included depending on their general design and then, a presentation of the correlation between skin and bone parameters that were retrieved from each study.

Risk of bias in individual studies

We assessed the validity of the eligible studies using the following markers: healthcare providers, data collectors, and outcome adjudicators and proportion of patients lost to follow-up. The authors did not exclude any study from the review or any subsequent analyses based on the risk of bias. They also did not plan sensitivity or subgroup analyses related to the bias assessments.

Additional analyses

No additional analyses such as sensitivity analysis, subgroup analysis, or meta-regression were planned *a priori*.

Table 1. Characteristics of the included studies

Study	Full title	First author	Journal	Date of publication	Number of patients	Age (range; mean; SD)	Gender F/M	Time of inclusion
1	Association between skin thickness and bone density in adult women	Patrícia de Paula Yoneda	Anais Brasileiros de Dermatologia	2011	140	57 (NR; NR; 10.9)	140/0	2008 - 2010
2	Can dermal thickness measured by ultrasound biomicroscopy assist in determining osteoporosis risk?	Perri E. Cagle	Skin Research and Technology	2007	98	NR (30-88; NR; NR)	98/0	2002 - 2003
3	Evaluation of Osteoporosis Using Skin Thickness Measurements	Rajesh Patel	Calcif Tissue Int	2007	603	NR (20–81; NR; NR)	603 / 0	NR
4	Effects of Aging and Postmenopausal Hypoestrogenism on Skin Elasticity and Bone Mineral Density in Japanese Women	Sumino H	Endocrine Journal	2004	38	NR (48-71; 55.7; 5.9)	38 / 0	NR
5	Relationship between bone mass density and tensile strength of the skin in women.	Piérard GE	European Journal of Clinical Investigation	2001	100	NR (NR; NR; NR)	100 / 0	NR
6	Limited value of ultrasound measured skin thickness in predicting bone mineral density in peri- and postmenopausal women	Eero Varila	Maturitas	1995	60	NR (53-56; NR; NR)	60 / 0	NR
7	Skin thickness in patients with osteoporosis and controls quantified by ultrasound A scan.	Pedersen H	Skin Pharmacology	1995	40	NR (NR; NR; NR)	40 / 0	NR
8	Skin Thickness does not Reflect Bone Mineral Density in Postmenopausal Women	Smeets AJ	Osteoporosis International	1994	94	NR (45-60; 52.7; 2.9)	94 / 0	NR
9	Relationship between skin collagen and bone changes during aging.	Castelo-Branco C	Maturitas	1994	76	NR (21-73; 43,77; 14.15)	76 / 0	NR
10	Is a low skinfold thickness an indicator of osteoporosis?	Orme SM	Clinical Endocrinology	1994	206	NR (NR; NR; NR)	206 / 0	NR
11	Relationships between bone and skin atrophies during aging	Chappard D	Acta Anat	1991	133	61.7 (17-94; NR; 16.3)	133 / 0	NR
12	A study of the decrease of skin collagen content, skin thickness and bone mass in the postmenopausal woman	Brincat M	Obstetrics & Gynecology	1987	148	NR (NR; 51; 7.9)	148 / 0	NR
13	Senile osteoporosis and collagen loss in skin	Balasubramaniam P	Singapore Medical Journal	1977	45	NR (55-81; NR; NR)	NR	NR
14	The relationship between skin and cortical bone thickness in old age with special reference to osteoporosis and diabetes mellitus: a roentgenographic study.	Meema HE	J Gerontol	1969	193	NR (NR; NR; NR)	193 / 0	NR

Table 2. Types of interventions performed on the participants

Study	First author, year of publication	Type of skin measurement	Anatomical site of skin measurement	Device	Type of bone measurement	Anatomical site of bone measurement	Device
1	**Yoneda et al., 2011**	Skin thickness	Hand	Pachymeter	Bone mineral density *(T-score)*	Femoral neck, total femur and lumbar spine	*Hologic Discovery bone densitometer*
2	**Cagle et al., 2007**	Skin thickness	Forearm	Echograph	Bone mineral density *(T-score)*	Femoral neck	*GE Lunar Prodigy DXA device*
3	**Patel et al., 2007**	Skin thickness	Forearm	Echograph	Bone mineral density *(T-score)*	Distal radius, femoral neck and lumbar spine	*Hologic QDR-4500 system and Osteometer DTX-200 peripheral DXA*
4	**Sumino et al., 2004**	Skin elasticity	Forearm	Vacuum	Bone mineral density *(g/cm2)*	Lumbar spine	*DXA; QDR- 1000W, Hologic*
5	**Piérard et al., 2001**	Skin elasticity	Forearm	Vacuum	Bone mineral density *(g/cm2)*	Femoral neck and lumbar spine.	*NR*
6	**Varila et al., 1995**	Skin thickness	Forearm / abdomen / leg	Echograph	Bone mineral density *(T-score)*	Distal radius, femoral neck and lumbar spine	*DXA, Norland XR-26*
7	**Pedersen et al., 1995**	Skin thickness	Hand / forearm / arm	Echograph	Bone mineral density *(g/cm2)*	Distal radius and lumbar spine	*BMC-LAB22s, Novo Diagnostics System and 125I, NovoGT, Novo Diagnostic System*
8	**Smeets et al., 1994**	Skin thickness	Forearm / arm	Echograph	Quantitative computed tomography *(mg/ml CallA)* and Bone mineral density *(mm A1 equivalent/mm3)*	Lumbar spine	*Somatom Plus CT scanner and standardized PA / L radiographs*
9	**Castelo-Branco et al., 1994**	Skin collagen	Abdomen	Biopsy	Bone mineral density *(g/cm2)*	Lumbar spine	*Lunar DP3 dual-photon absorptiomete*
10	**Orme et al., 1994**	Skin thickness	Hand	Caliper	Bone mineral density *(T-score)*	Femoral neck and lumbar spine	*DEXA Lunae corporation*
11	**Chappard et al., 1991**	Skin thickness	Hand	Caliper	Bone mineral density *(g/cm2)*	Lumbar spine	*Hologic QDR-1000*
12	**Brincat et al., 1987**	Skin thickness	Forearm	Radiograph	Metacarpal index and bone mineral content *(g/cm2)*	Second metacarpal (*metacarpal index*) and forearm (*bone mineral content*)	*Standardized PA / L radiographs*
13	**Balasubramaniam et al., 1977**	Skin collagen	Hand	Biopsy	Trabecular pattern *(Singh index)*	Femoral neck	*Standardized PA / L radiographs*
14	**Meema et al., 1969**	Skin thickness	NR	Radiograph	Cortical thickness *(mm)*	Proximal end of the radius shaft	*Standardized PA / L radiographs*

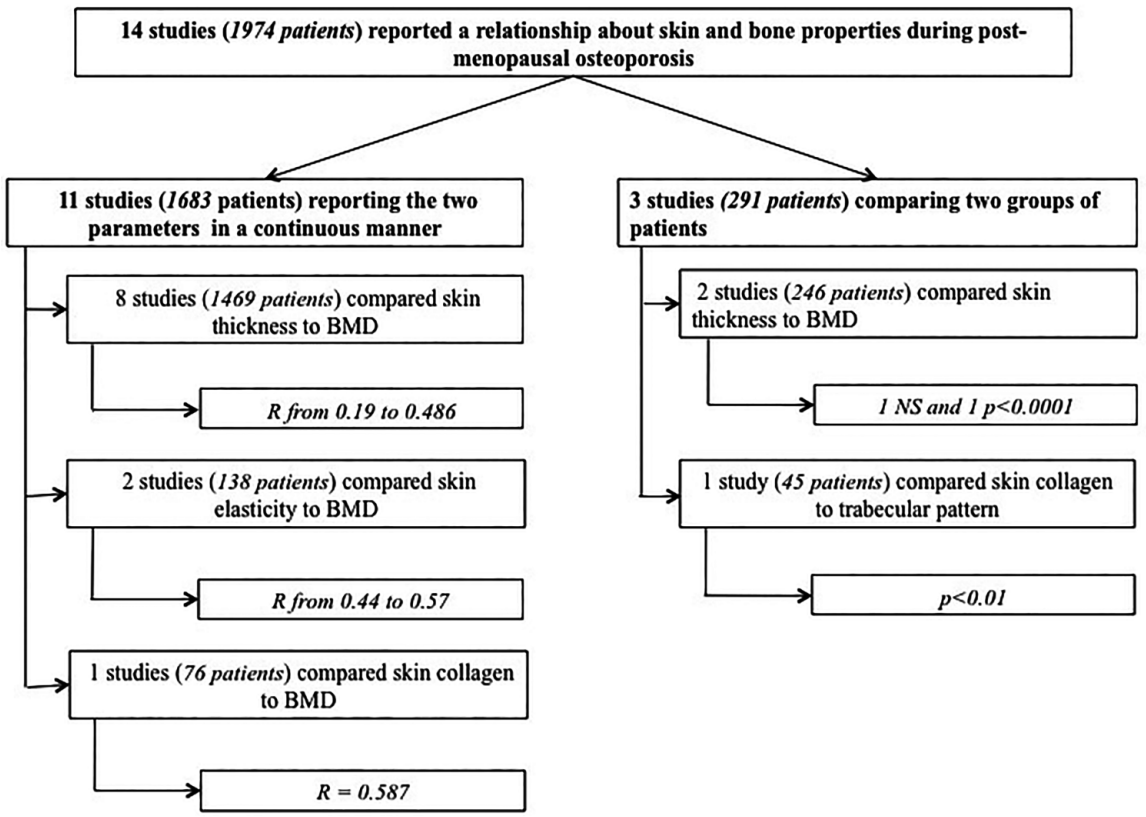

Fig. 2 Types of bone and skin parameters compared in each study and importance of the relationship found between the different parameters tested.

Results

Selection of the included studies

We identified 14 studies for inclusion in the review (Fig. 1).[14–27] The search of Medline, EMBASE and the Cochrane Library provided 1577 citations (976, 563 and 38 respectively). After exclusion of 601 duplicates, we discarded 965 articles: 944 from the title because they were clearly not on the subject and 21 from the abstract (four were clearly not on the subject, five considered other bone disease, six were not in English or in French, and six were reviews). In addition, we identified three additional studies that met criteria for inclusion by checking the references of relevant papers.

Characteristics of the included studies

Among the 14 studies included in the final analysis, all had a prospective design. No study was published between 1950 and 1959, one was published between 1960 and 1969, one was published between 1970 and 1979, one was published between 1980 and 1989, six were published between 1990 and 1999, four were published between 2000 and 2010 and finally, one was published after 2010. They involved 1974 patients in total. All were women. Mean age was 53.6 years (not reported [NR] in eight studies). Among these patients, 1054 were postmenopausal women and were 337 premenopausal (NR in 5 studies). In addition, 221 women were diagnosed with osteoporosis while 210 were not (NR in 10 studies) (see Table 1).

Interventions

All the participants underwent an analysis of skin and bone parameters (Table 2). The skin parameters tested in the included studies were: an estimation of skin thickness in 10 studies (1715 patients), an estimation of skin elasticity in two studies (138 patients) and an estimation of the collagen content in two studies (121 patients). Several devices were used to assess the skin thickness: radiographs,[27,32] calipers,[23,24] echographs[16,17,19–21,42] and a pachymeter.[15] The anatomical site of the measurement of the skin parameter was: the hand only in five studies or 524 patients; the forearm only in five studies or 987 patients; the abdomen only in one study or 76 patients; and several sites in three studies or 194 patients (NR in one study). The bone parameters tested in the included studies were: an estimation of BMD in 10 studies or 1494 patients (expressed as T-score in five studies or 1107

Table 3. Results of the studies comparing two different groups of participants – osteoporotic and non-osteoporotic

Study	Type of skin measurement	Type of bone measurement	Number of patients (osteoporotic – non osteoporotic)	Type of study	Primary outcome	Results
Pedersen H, 1995	Skin thickness	Bone mineral density (grams of hydroxyapatite)	40 (20 – 20)	Case-control study	Difference of skin thickness between 2 groups	No statistically significant difference ($p>0.05$)
Orme SM, 1994	Skin thickness	Bone mineral density (T-score)	206 (141 – 65)	Case-control study	Difference of skin thickness between 2 groups	1.6 +/- 0.4 mm Vs 1.8 +/- 0.3 mm ($p<0.0001$)
Balasubramaniam P, 1977	Skin collagen	Trabecular pattern (Singh index)	45 (23 – 22)	Case-control study	Correlation between the amount of skin collagen and osteoporosis.	Statistically significant difference ($p<0.01$)

Table 4. Results of the studies comparing skin and bone parameters in a continuous manner

Study	Type of skin measurement	Type of bone measurement	Number of patients	Type of study	Primary outcome	Results
Yoneda et al., 2011	Skin thickness	Bone mineral density (T-score)	140	Cross-sectional study	Correlation between skin thickness and BMD	R = 0.34 *(P<0.01)*
Cagle et al., 2007	Skin thickness	Bone mineral density (T-score)	98	Cross-sectional study	Correlation between skin thickness and BMD	R = 0.304 *(P=0.001)*
Patel et al., 2007	Skin thickness	Bone mineral density (T-score)	603	Cross-sectional study	Correlation between skin thickness and BMD	R = 0.21 – 0.29 *(P < 0.0001)*
Varila et al., 1995	Skin thickness	Bone mineral density (T-score)	60	Cross-sectional study	Correlation between skin thickness and BMD	R = 0.19 - 0.24 *(p=NR)*
Smeets et al., 1994	Skin thickness	Quantitative computed tomography (mg/ml CallA) and Bone mineral density (mm A1 equivalent/mm3)	94	Cross-sectional study	Correlation between skin thickness and BMD	R= NR *(p=NS)*
Chappard et al., 1991	Skin thickness	Bone mineral density (g/cm2)	133	Cross-sectional study	Correlation between skin thickness and BMD	R = 0.364 for vertebral BMD *(p<0.0001)* R = 0.486 for femoral BMD *(p<0.0001)*
Brincat et al., 1987	Skin thickness	Metacarpal index and bone mineral content	148	Cross-sectional study	Correlation between skin thickness and metacarpal index and bone mineral content	NS for BMC 3cm R = 0.24 for BMC 8cm *(p<0.05)*
Meema et al., 1969	Skin thickness	Cortical thickness	193	Cross-sectional study	Correlation between skin thickness and cortical thickness	R = 0.28 in the diabetic group *(p<0.05)* R = 0.33 in the non-diabetic group *(p<0.01)* R = 0.37 *(p<0.05)* in the non-diabetics with vertebral compressions
Sumino et al., 2004	Skin elasticity	Bone mineral density (g/cm2)	38	Cross-sectional study	Correlation between skin elasticity and BMD	R = 0.44 *(p<0.01)*
Piérard et al., 2001	Skin elasticity	Bone mineral density (g/cm2)	100	Cross-sectional study	Correlation between skin tensile strength and BMD	R = 0.48 in the hip *(p<0.05)* R = 0.57 in the femoral neck *(p<0.01)* R = 0.46 in the lumbar spine *(p<0.05)*
Castelo-Branco et al., 1994	Skin collagen	Bone mineral density (grams of hydroxyapataite)	76 (33 – 42)	Cross-sectional study	Correlation between skin collagen and BMD	R = 0.587 *(p<0.000l)*

patients and in g/mm^3 in five studies or 387 patients); a quantitative computed tomography in one study or 94 patients; the metacarpal index in one study or 148 patients; the trabecular pattern (Singh index) in one study or 45 patients; and the cortical thickness in one study or 193 patients.

Primary and secondary outcomes (Fig. 2)

On the one hand, three studies included two groups of participants – osteoporotic and non-osteoporotic – in order to compare skin parameters between them (Table 3). Among these studies, two found a significant difference between the two groups and one did not. On the other hand, eleven studies included one population of interest and compared skin and bone parameters in a continuous manner (Table 4). Among these studies, eight compared dermal thickness to BMD: seven of them found a significant correlation (*R* from 0.19 to 0.486) and one did not. Two studies compared skin elasticity with BMD and both found a significant correlation (*R* from 0.44 to 0.57). Finally, one study compared skin collagen to BMD and found a significant correlation (*R* = 0.587).

Synthesis of results

The included studies allowed the drawing of a path from the skin to the bone. Indeed, there are sufficient data to confirm that the degradation of certain skin parameters is correlated with the degradation of certain bone parameters in postmenopausal osteoporosis. The difficulty lies in the fact that the importance of this correlation varies greatly

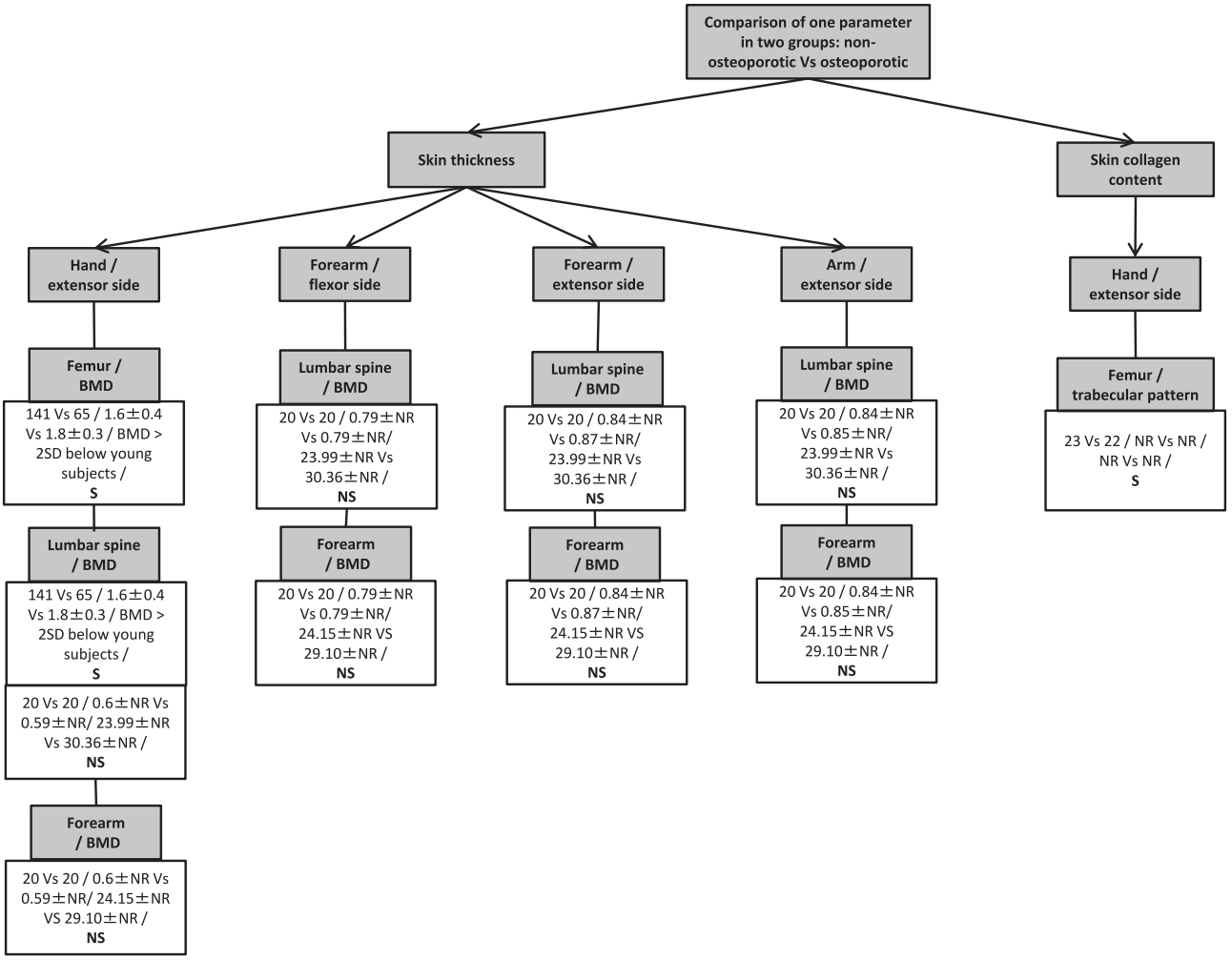

Fig. 3 Results extracted from the studies comparing one skin parameter in two groups (non-osteoporotic vs. osteoporotic), such as skin thickness[20,23] and skin collagen content,[26] depending on the anatomical sites where the measurements were made (number of patients/skin results/bone results/correlation).

between the different parameters that were tested and the location where they were performed.

First, three studies indicated that several skin parameters would allow the clinician to separate two groups of patients: those with osteoporosis and those without (Fig. 3). Among these parameters, the ones that were reported with the most relevant correlation were the skin thickness measured at the extensor side of the hand[23] and the skin collagen content extracted from the extensor side of the hand.[26] However, one of these three studies could not confirm the aforementioned results for skin thickness measured at the extensor side of the hand and also found no impact of skin thickness measured at the forearm.[20]

Second, several studies reported a correlation between several skin and bone parameters that could allow an estimation of a bone parameter from a skin parameter. Indeed, skin elasticity measured on the extensor aspect of the forearm (Fig. 4) could be used to estimate BMD at the lumbar spine, hip and femoral neck.[14,18] Also, skin thickness on the extensor aspect of the hand and on the flexor side of the forearm (Fig. 5a) could be used to estimate several sites of BMD.[15,16,19,25,27] However, skin thickness on the arm extensor aspect has not been reported to be correlated with any alteration of bone properties.[21] Also, skin thickness at the abdomen or at the leg (Fig. 5b) has not been reported to be correlated to any alteration.[19] Finally, skin collagen harvested from the abdomen (Fig. 5b) could not be used to estimate BMD at the lumbar spine.[22]

Discussion

Biochemical connections between skin and bone tissues exist because both tissue types are mainly composed of

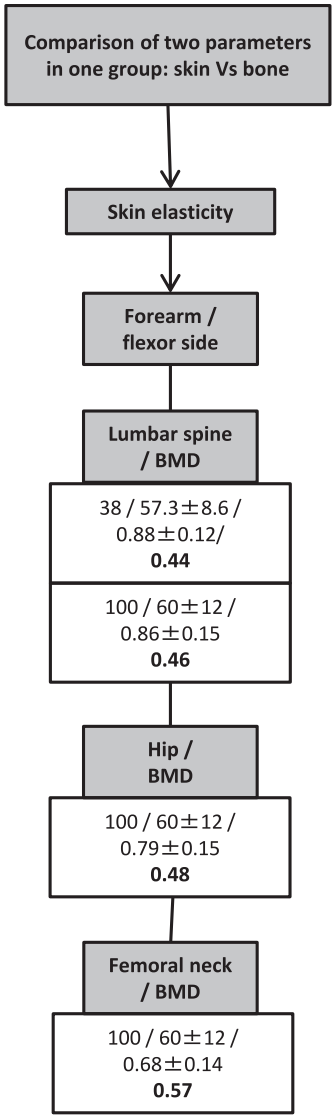

Fig. 4 Results extracted from the study comparing two parameters (skin elasticity and bone mineral density) in one population, depending on the anatomical sites where the measurements were made (number of patients/skin results/ bone results/correlation).[14,18]

collagen.[6,28] Indeed, many authors have tried to verify this observation with various clinical trials. In this systematic review of every study reporting relationships between skin and bone parameters in women with postmenopausal osteoporosis, we have confirmed the hypothesis of a certain correlation between the alteration of skin and bone tissues with age. Hence, measurement of certain skin parameters could be performed in order to estimate bone parameters.

The general process of ageing could explain the origins of the correlation between the alterations of skin and bone parameters. In fact, ageing is a common process within a population, and takes place in every subject. One of the most representative ageing changes is the alteration of the mechanical properties of the tissues. For the skin, bone and other organs, these properties are mostly determined by the connective tissue. Collagen is the main protein in the connective tissue and is widely distributed throughout the body. Skin collagen is comparable with collagen in other locations of the human body, and it is reasonable to assume that ageing skin collagen undergoes some of the same modifications as collagen from other sites.[29] Bone is a metabolically active tissue composed of an organic matrix made up of collagen and several non-collagenous proteins (osteocalcin, osteonectin, etc.) and an inorganic component (hydroxyapatite). Hence, assuming that all the collagen of the body will age equally, it is possible that skin and bone will age in the same manner, especially in postmenopausal osteoporosis.[10]

Bone mass and skin collagen content share comparable regressive changes during ageing. Some authors have pointed out that skin collagen is influenced by the loss of oestrogen production by the ovaries and that skin collagen content decreases in the postmenopausal years.[30–33] Clinically, ageing skin shows fine wrinkling, thinning – reflecting atrophy of the collagenous dermis – and poor wound healing. Examination of age-related changes in the dermis by light and electron microscopy has demonstrated disorganization of the elastic fibre network together with a decrease in the number of collagen fibre bundles.[34,35] Moreover, ageing is correlated with loss of bone mass.[36–38] It seems that the conclusions drawn by Albright et al 50 years ago are valid and that bone loss accelerates in women when ovarian failure occurs, and the event of global gonadal function decline at the menopause induces a major risk for osteoporosis in those women.[39–41] These observations support our findings of a certain correlation between the parameters of the skin and the parameters of the bone in postmenopausal osteoporosis.

This systematic review confirms that skin parameters could be of help in differentiating two types of population: osteoporotic and non-osteoporotic. However, the results of this study must be interpreted cautiously for various reasons. First, the correlation between the diminution of skin thickness and the diminution of bone mineral density in the investigated population was moderate at best. And the correlation between the diminution of skin elasticity and bone mineral density was only slightly stronger. Second, different methodologies have been used to assess the skin and bone parameters. The main skin parameter that was tested was biophysical – skin thickness – and several devices were used to assess it: radiographs,[27,32] calipers,[23,24] echographs[16,17,19–21,42] and a pachymeter.[15] Furthermore, the skin thickness obtained with these various methods has been compared with several biophysical bone parameters: BMD[15–17,19,20,23,24], bone mineral content[21,32] and cortical thickness.[27] The other skin parameter that was tested was

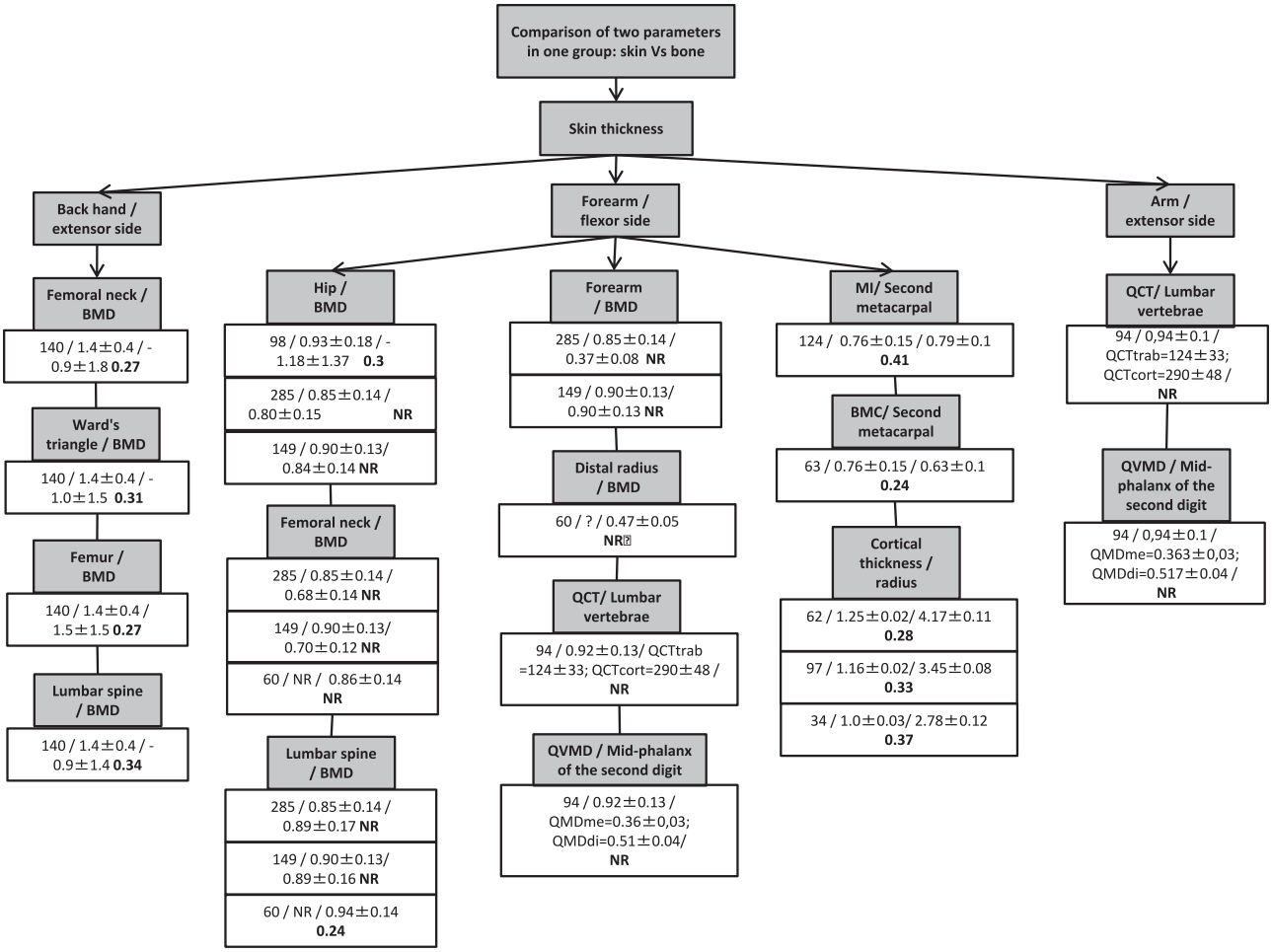

Fig. 5A Results extracted from the studies comparing two parameters (skin thickness and certain bone properties) in one group, depending on the anatomical sites where the measurements were made (number of patients/skin results/bone results/correlation).[15–17,19,21,25,27]

also biophysical – skin elasticity – and it was compared with a biophysical bone parameter, BMD.[14,18] The last skin parameter that was tested was biochemical – the collagen content of the skin – and it was compared with a biophysical bone parameter: BMD in one case[22] and trabecular pattern in the other. Third, several of the parameters used to test the bone are now obsolete – cortical thickness and the Singh index for instance – and they may jeopardize the comparison with other studies that used more recent parameters. Finally, the studies included in this review were chosen to identify a correlation between two parameters: one of skin and one of bone. The goal of those epidemiological studies was that a diminution of a skin parameter would make the clinician suspect osteoporosis. To the best of our knowledge, there is no data that would allow an algorithm to be designed that would allow estimation of the alteration of one parameter – skin thickness for instance – from another one – BMD for instance. That would be the next step. Furthermore, we found that most of these studies reported a correlation between certain skin and bone parameters during postmenopausal osteoporosis. But ultimately, none of these alone can predict the risk of fracture, which we want to prevent in this population. Indeed, the risk of osteoporosis is multi-factorial and includes biotypes and environmental conditions that may not be taken into consideration with this method.

We acknowledge several limitations to the study itself. First, the studies that were included in the analysis do not lend themselves to comparison, nor do they make it possible to combine data to reach a conclusion. Skin thickness was measured in many different sites by different methods and bone was assessed by BMD, plain films of the spine, and carpal density and thickness. Second, the timeframe of inclusion is very large and the methods used to test skin and bone parameters may have changed. In studies predating 1990, Dual Energy X-Ray was not used to measure BMD, and old methods lacking accuracy were employed, including metacarpal

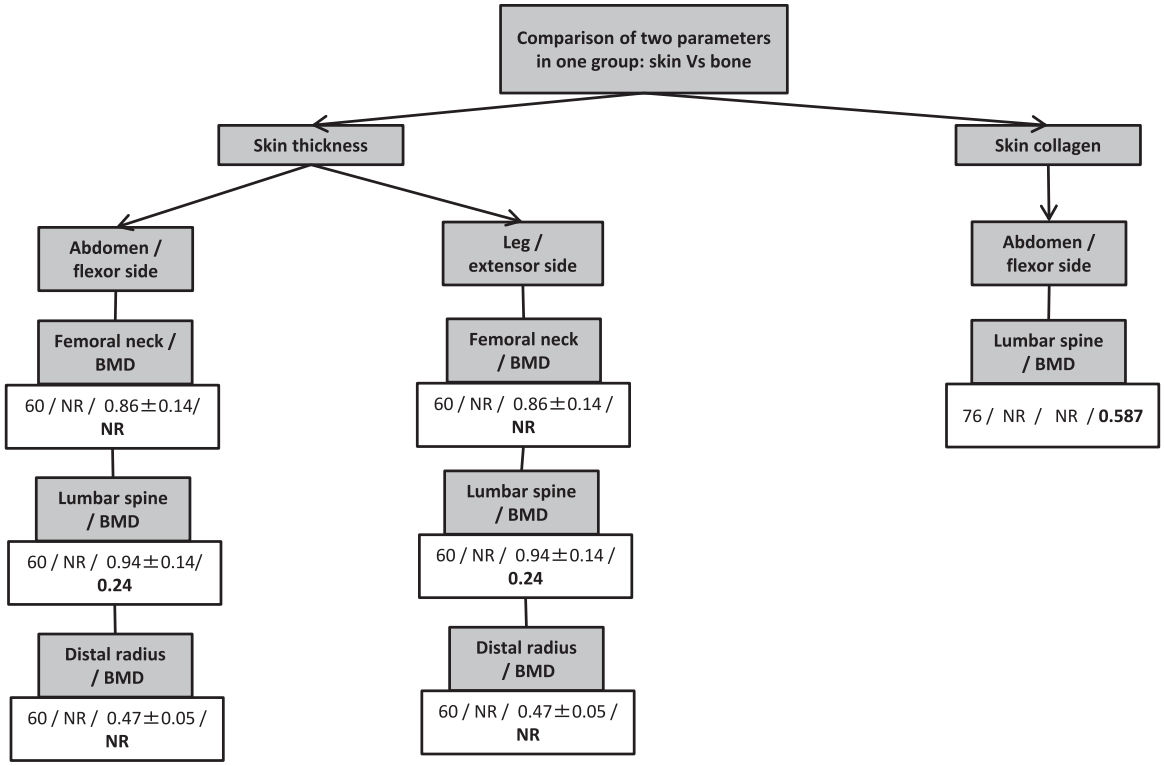

Fig. 5B Results extracted from the study comparing two parameters (skin thickness and bone mineral density) in one group, depending on the anatomical sites where the measurements were made (number of patients/skin results/bone results/ correlation).[19,22]

index, trabecular pattern by Singh index and cortical thickness by radial shaft radiograph. Third, despite a large timeframe, only 14 studies were found – this represents a very low number. Furthermore, the 14 included studies included various designs and the parameters tested were very different, which could have led to misinterpretations. Fourth, most of the studies included in the review are more than 5 years old. This reflects the fact there was a trend to try to correlate skin and bone ageing several decades ago, but the correlations were moderate. Hence, this hypothesis began to interest researchers less and less despite the fact that the correlation, although modest, seemed real. Recently, interest in this medical hypothesis has been renewed for a specific population – contra-lateral hip fractures.[43] Fifth, the selection of the studies included in our study represents another limitation. It is possible that studies performed during the interval but not published in English or not published at all were not included in this review. Given the fact that this kind of study usually presents inconclusive results, it represents a bias of our current study. Finally, because of the great heterogeneity of the results reported in all the included studies, no meta-analysis was carried out and the results are presented as extracted, limiting their interpretation.

Conclusion

We found a majority of studies that reported a correlation between skin and bone parameters in postmenopausal osteoporosis. However, only a limited number of parameters were tested in each study. Now, overall tests are still needed to improve the understanding of the concomitant modifications of skin and bone in postmenopausal osteoporosis.

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