Clinical Usefulness of Urinary Hydroxyproline as a Biochemical Marker of Bone Resorption

Üriner Hidroksiprolinin Kemik Rezorbsiyonu Biyokimyasal Belirleyicisi Olarak Klinik Yararlılığı

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Anahtar kelimeler: Kemik rezorpsiyonu, kemik rezorpsiyon markerleri, üriner hidroksiprolin

SUMMARY: Hydroxyproline is a modified amino acid that is metabolic product of collagen breakdown. Type I collagen is a major product of osteoblast. During bone resorption, hydroxyproline may be released either free or with fragments of the collagen molecule attached. It is not reutilized in collagen synthesis. Hydroxyproline is also liberated by the breakdown of complement and nonskeletal collagen. Urine hydroxyproline as a marker of bone resorption has long been in use for years. However, it is highly metabolized before being excreted and urinary excretion of hydroxyproline represents only about 10% of total collagen catabolism. Urinary hydroxyproline is the commonly used marker of bone resorption, but it lacks sensitivity and specificity. If the limitations can be dealt with appropriately, hydroxyproline measurements can provide a reasonable means of assessing metabolic activity.

Key words: Bone resorption, bone resorption marker, urinary hydroxyproline

Bone metabolism is characterized by a dynamic and continuous process to maintain a balance between the resorption of old and injured bone initiated by osteoclasts, and the formation of new bone under the control of osteoblasts. This continuous degradation and formation of bone throughout life is termed bone remodelling or bone turnover. The balance between bone resorption and bone formation, which is altered in most metabolic diseases is important in the maintenance of normal bone turnover.

The state of the skeleton can be assessed by a wide variety of procedures, including histomorphometry and measurement of calcium fluxes. Histomorphometry is invasive, expensive, has a long turnaround time, and is limited to a single skeletal site, iliac crest. Measurement of calcium fluxes is technically difficult. In recent years, additional techniques for assessing the skeleton, including improved radiological and densitometric procedures and newer computer-assisted imaging methods for bone, have been developed. However, these methods are also expensive and inconvenient and cannot be performed at sufficiently frequent intervals to reveal dynamic changes in the skeleton. This void has been filled with the identification of biochemical markers of bone remodeling, the monitoring of which is noninvasive, inexpensive, and can be repeated often. Most of the new biochemical markers have been targeted for use in assessing bone resorption since bone loss due to metabolic bone disease is the more important clinical factor to monitor and evaluate in bone disease. Biochemical markers of bone resorption that reflect osteoclast activity and/or collagen degradation provide a new and potentially important clinical tool for the assessment and monitoring of bone metabolism. Metabolic products of bone collagen breakdown have been the recent focus of laboratory methods designed to assess bone resorption. Urine hydroxyproline as a marker of collagen breakdown has been in use for years.

Hydroxyproline is a modified amino acid that is derived from proline by a posttranslation hydroxylation occurring within the peptid chain. Hydroxyproline is found mainly in collagens, comprising about 13% of the amino acid content of these proteins. Because free hydroxyproline liberated from the breakdown of collagen is not
reutilized for collagen biosynthesis, most of the endoge­
nous hydroxyproline present in biological fluids is
derived from the degradation of various forms of colla­
gen\textsuperscript{14,15}. About 90% of the hydroxyproline released by
the breakdown of collagen in the tissues, especially dur­
ing bone resorption is degraded to free amino acid form
that readily passes through the glomerulus. It is eventu­
ally completely oxidized and catabolized in the liver to
urea and carbon dioxide\textsuperscript{16,17}. The remaining 10% of the
hydroxyproline is released in small polypeptide chains
that pass through the glomerulus and are excreted in
urine without any further metabolism\textsuperscript{1,3,5}.

Since half of human collagen resides in bone, excretion
of hydroxyproline in urine is regarded as a marker of
bone resorption\textsuperscript{3,4,14}. The major component of bone
matrix is Type I collagen, which is rich in hydroxypro­
line\textsuperscript{6,18}. Although some Type I collagen is present in
nonskeletal tissues, bone has a much higher proportion
and a much higher turnover\textsuperscript{5}. Approximately 50% of ur­
inary hydroxyproline is derived from bone collagen
breakdown\textsuperscript{5,19}.

Although hydroxyproline constitutes a substantial pro­
portion of the amino acid content of Type I bone colla­
gen and measurement of this amino acid has been used
to monitor bone resorption\textsuperscript{1}, the urinary total hydrox­
proline represents only a small fraction of total collagen
catabolism, and this method is not very specific to Type
I bone collagen\textsuperscript{6,13,14,20}. There are a number of issues that
can lead to a lack of tissue specificity\textsuperscript{1}. Hydroxyproline
is also liberated by the breakdown of complement\textsuperscript{5}. The
\textit{C}1\textit{q} fraction of complement contains a structural region
that is similar to collagen, containing significant amounts
of hydroxyproline and could account for up to 40% of
urinary hydroxyproline\textsuperscript{16,21}.

For this reason inflammatory conditions can cause dra­
matic increases in urine excretion of hydroxyproline\textsuperscript{1,22}.
Hydroxyproline is also found in nonskeletal collagen
sources including Type II collagen of cartilage and
skin\textsuperscript{12}. It is also released by the breakdown of procolla­
gen I extension peptides\textsuperscript{5,19}. Hydroxyproline from pro­
collagen I aminoterminal propeptide (PINP extension
peptide) probably reflects bone formation rather than
bone resorption\textsuperscript{1,22}. Hydroxyproline levels are also influ­
cenced by dietary intake of gelatin containing food prod­
ucts\textsuperscript{1,12,22}. An overnight fast, however, reportedly elimi­
nates the effects of dietary hydroxyproline\textsuperscript{1,13}. A major
problem has been that, apart from dietary sources,
References


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