Hormone and Bone Tests May Predict Progression of Coronary Artery Calcification in Patients on Dialysis

Many patients with chronic kidney disease (CKD) and end stage renal disease exhibit coronary artery calcification as well as low bone mass. A new study published in the Journal of the American Society of Nephrology now shows that monitoring bone loss in dialysis patients may provide early warning signs of cardiovascular problems.

"Coronary artery calcification progresses inexorably in patients on dialysis, and these patients have mortality rates related to cardiovascular events worse than many cancers," said lead author Hartmut Malluche, MD, FACP, of the University of Kentucky. "The link between bone and vascular calcifications is a potentially very important avenue, and studies need to be done to find out whether prevention of bone loss will reduce progression of vascular calcifications."

Malluche and his team noted that no information is available on the use of noninvasive bone mass assessments—such as dual energy x-ray absorptiometry or quantitative computed tomography—for predicting progression of coronary artery calcification. There’s also little information on how traditional and novel serum biochemical parameters relate to progression.

To fill these gaps, the researchers conducted tests to analyze abnormalities in blood, bone, and heart vessels in 213 patients on dialysis over a 1-year period. About 80% of the patients had measurable coronary artery calcification at baseline, and almost 50% had levels that confer a high risk for cardiovascular events. Independent positive predictors of baseline coronary artery calcification included coronary artery disease, diabetes, dialysis vintage, fibroblast growth factor-23 concentration, and age.

Bone mineral density of the spine measured by quantitative computed tomography was an inverse predictor. Contrary to other studies, the investigators did not find a sex difference in baseline coronary artery calcification. Baseline coronary artery calcification was associated with a higher frequency of coronary and vascular events over the 1-year period. Independent positive predictors of progression of calcification included coronary artery disease, diabetes, dialysis vintage, fibroblast growth factor-23 concentration, and age.

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Applications to Nephrology fellowships have declined significantly since 2010, yet the number of training opportunities has increased. Nephrology fellowship programs increased from 127 in 2000 to 147 in 2013, and the number of fellows in the first or second year of training jumped from 626 to 930 in that time period. However, the number of applicants participating declined from 376 in 2010 to an all-time low of 254 in the Match for the 2015 appointment year.

The Nephrology Match was designed to provide applicants and program directors opportunities to thoughtfully consider all options. Position offers to applicants outside the Match sometimes exert pressure on applicants to make early decisions, and degrade confidence in the integrity of the Match process.

As the sponsoring organization for the Match, the American Society of Nephrology (ASN) convened a Nephrology Match Task Force in January 2015 to review principles and practices of the Match and recommend improvements. The Task
Hormone and Bone Tests

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artery calcification was lower in patients who reported exercising compared with those who did not, which is a novel find-

ing of the factors that contribute to the prevalence of coronary artery calcification in patients on dialysis, they don’t neces-
sarily help clinicians predict which pa-
tients will experience progression.

Dr. Malluche and his colleagues found that at 1 year, independent risk factors for progression of coronary artery calci-
fication were age, baseline total or whole
parathyroid hormone level greater than 9
times the normal value, and osteopo-
rosis. Bone mineral density of the total
hip, femoral neck, and spine was shown
for the first time in dialysis patients to
 correlate with baseline coronary artery
calcification as well as a diagnosis of os-
teoporosis by t scores.

“We discovered that high parathyroid
hormone and the consequential bone loss are major risk factors for progression of vas-
cular calcifications,” Malluche said. “These
two factors were heretofore not appreci-
ated and were independent from traditional
known risk factors.” The researchers noted
that previous studies that started para-
thyroid hormone levels and increased risk of vas-
cular disease in CKD,” said Paul Miller,
MD, who was not involved with the re-
search and is a Distinguished Clinical
Professor of Medicine at the University of
Colorado Health Sciences Center and the
Medical Director of the Colorado Center
for Bone Research, in Lakewood.

Study co-authors include Gustav
Blomquist, MD, Marie-Claude Monier-
Faugere, MD, Thomas Cantor, and Dan-
iel Davenport, PhD.

Disclosures: The authors reported no fi-
nancial disclosures.

The article, entitled “High Parathyroid
Hormone Level and Osteoporosis Predict
Progression of Coronary Artery Calcifica-
tion in Patients on Dialysis,” is available at
http://jasn.asnjournals.org/content/early/
2015/04/01/ASN.2014070686.abstract.

ASN Initiatives

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1. ASN should continue its relationship with the National Resident Matching Program’s (NRMP’s) Specialties Match Service (SMS).

Task force discussions centered on the in-
terests of applicants and the need to iden-
tify excellent candidates and ensure the best fit between programs and candidates. Members concluded that continued par-
ticipation in the Match offers the best way to protect the rights of both the applicants and programs.

Recommendation 2: All Accreditation Council for Graduate Medical Education (ACGME)-

accredited nephrology training programs should participate in the NRMP Match and offer all positions through the Match.

As the number of Nephrology fellowship ap-
licants has declined, the number of Neph-
rology positions filled outside the Match has increased. This has created frustration among training program directors and un-
desired for applicants and program directors’ trust in the Match. This also risks exacerbat-
ing declines in Match participation.

Task Force members recommended Nephrology adopt an “all-in” policy, in which all accredited training programs par-
ticipate and all positions must be filled in the NRMP Match, concluding that this policy
would best serve the fellowship applicants, training programs, and the discipline.

The Road Ahead

While outside the scope of this task force, broadening the appeal of nephrology is a priority for ASN: since 2010, the society has dedicated considerable resources to increasing interest in nephrology careers. The changes to the Match will help ensure that nephrology training programs con-
tinue to provide excellent candidates with high-quality educational experiences. The next generation of nephrologists must fuel advances to the complex and challenging care of patients with kidney disease.

To provide feedback or send questions about the Match, please write nephrologymatch@as-
online.org. More information on the Match is available at www.asn-online.org/match.

Recommendation 3: Nephrology

programs should retain the ability to offer multiple tracks but offer only three options: “Clinical,” “Research,” and “Other.”

Internal medicine specialties vary in use of program tracks in the Match. Discussions centered on which approaches are most supportive and least confusing for applicants and programs, and noted that programs can “revert” unfilled positions to be filled from their rank list for cli-
tical tracks. The group universally recommen-
ded that diversity in program tracks should remain, but options reduced from four to three: “Clinical,” “Research,” and “Other,” eliminating the “Basic” and “Clinical” research designations. The ASN Council also unanimously approved this recommendation.

Assessing Program Size

One of the most complex issues discussed centered on how individual programs and institutions determine the number of train-
ing slots. In future publications, ASN will address this challenge and provide self-assess-
ment tools to help program leaders evaluate program size. During its retreat in May, the Nephrology Training Program Directors provided input regarding this challenge.

Table 1. ASN Nephrology Match Task Force

| Chair |
| Raymond C. Harris, MD, FASN |
| Ann and Roscoe Robinson Professor of Medicine |
| Chief, Division of Nephrology |
| Vanderbilt University School of Medicine |

| Members |
| Nancy Day Adams, MD |
| Professor of Medicine |
| Chief, Division of Nephrology |
| Nephrology Training Program Director |
| University of Connecticut School of Medicine |
| Sharon G. Adler, MD, FASN |
| Professor of Medicine |
| Associate Chief, Division of Nephrology |
| David Geffen School of Medicine |
| University of California at Los Angeles |
| Nephrology Training Program Director |
| Harbor UCLA Medical Center |
| Gregory L. Braden, MD |
| Professor of Medicine |
| Tufts University School of Medicine |
| Chief, Division of Nephrology |
| Nephrology Training Program Director |
| Baystate Medical Center |
| Gary V. Desir, MD |
| Professor of Medicine |
| Interim Chair, Department of Medicine |
| Yale University School of Medicine |
| Chiyuan Hsu, MD |
| Professor of Medicine |
| Chief of Nephrology |
| University of California, San Francisco, School of Medicine |

The findings indicate that important information can be gained from moni-
toring parathyroid hormone levels and bone mass in patients on dialysis, to nor-
only assess bone health but cardiovascular health as well. Additional controlled pro-
spective studies are needed to evaluate the effects on coronary artery calcification of
different therapies that are marketed to target osteoporosis or parathyroid hor-
mones.

“This study adds a different perspec-
tive on mechanisms associated with vas-
cular calcification in CKD that is different from the previously described associations of low bone turnover and low parathyroid hormone levels and increased risk of vas-
cular disease in CKD,” said Paul Miller,
MD, who was not involved with the re-
search and is a Distinguished Clinical

Mark D. Okusa, MD
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Mark G. Parker, MD
Clinical Associate Professor |
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See more at http://jasn.asnjournals.org/content/ear-
lv/2015/04/01/ASN.2014070686.abstract.