Q&A column, 4/15

Editor: Frederick L. Kiechle, MD, PhD

Submit your pathology-related question for reply by appropriate medical consultants. CAP TODAY will make every effort to answer all relevant questions. However, those questions that are not of general interest may not receive a reply. For your question to be considered, you must include your name and address; this information will be omitted if your question is published in CAP TODAY.

Submit a Question

Lymph node retrieval in colon cancer

Maximum allowable dilutions

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Q. Why is the number 12 for lymph node retrieval in colon cancer protocol reporting not specific to the kind of resected specimens and whether a total colectomy was performed?

A. It is important to realize that the number 12 is not a magic number, and other cutoffs and parameters, like lymph node ratio, have been proposed as better prognostic indicators.[1-3] The idea of a cutoff is based on data that show that cases designated as stage II based on examination of fewer than 12 lymph nodes have worse outcomes than stage II cases based on examination of 12 or more lymph nodes.[3,4] At the practical level, it means the following:

- If fewer than 12 lymph nodes are retrieved, a more extensive search should be done, perhaps with acetone or other fat-clearing solutions.[5]
- The search for lymph nodes should not stop once 12 lymph nodes have been obtained, but special techniques such as acetone are perhaps not warranted once this number is achieved.
- It is well known that specimens from the rectosigmoid region and those obtained after neoadjuvant therapy typically have fewer lymph nodes.[6] If 12 lymph nodes are not obtained in these cases even after acetone treatment, the standard of care (from the pathology side) has been met.

I personally do not like the idea of having different cutoffs for different situations. Having one cutoff is one too many. If the limitations of certain kinds of specimens are taken into account and acetone treatment is done, the cutoff of 12 is fine for all situations. The utility of this cutoff at a practical level is to ensure a thorough search for lymph nodes. It is not a threshold to be used as a mark of failure or inferior work ethic, if a thorough search has been performed.

1. Chang YJ, Chang YJ, Chen LJ, Chung KP, Lai MS. Evaluation of lymph nodes in patients with colon cancer undergoing colon resection: a population-based study. World J Surg. 2012;36(8):1906–1914.
2. Sjo OH, Merok MA, Svindland A, Nesbakken A. Prognostic impact of

lymph node harvest and lymph node ratio in patients with colon cancer. *Dis Colon Rectum.* 2012;55(3):307–315.
3. Iachetta F, Reggiani Bonetti L, Marcheselli L, et al. Lymph node evaluation in stage IIA colorectal cancer and its impact on patient prognosis: a population-based study. *Acta Oncol.* 2013;52(8):1682–1690.
4. Baxter NN, Virnig DJ, Rothenberger DA, Morris AM, Jessurun J, Virnig BA. Lymph node evaluation in colorectal cancer patients: a population-based study. *J Natl Cancer Inst.* 2005;97(3):219–225.
5. Horne J, Bateman AC, Carr NJ, Ryder I. Lymph node revealing solutions in colorectal cancer: should they be used routinely? *J Clin Pathol.* 2014;67(5):383–388.
6. Wong SL. Lymph node counts and survival rates after resection for colon and rectal cancer. *Gastrointest Cancer Res.* 2009;3(2 suppl):S33–S35.

Sanjay Kakar, MD,
Professor, University of California, San Francisco
Benedict Yen Endowed Chair for Chief of Pathology
Veterans Affairs Medical Center, San Francisco
Member, CAP Cancer Committee

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Q. We are establishing a list of maximum allowable dilutions for our clinical chemistry analytes. Are you aware of any reference that would list absurd or invalid values for such analytes, i.e. the endpoint that would determine the most dilutions we would have to do for the highest possible value for that analyte?

A. Response to this question requires a brief review of the definition of analytical measurement range, its verification, and how it affects laboratory operations. All are regularly discussed and debated in laboratories during inspections.

- The analytical measurement range, as defined in the CAP's chemistry and toxicology checklist, is the range of results that the assay can report without any dilution or concentration. Verification of a manufacturer's stated AMR is detailed in checklist requirement CHM.13600. Essentially, the lower, middle, and upper ranges of the AMR must be validated. If material is not available to verify the AMR's exact upper limit, a statement from the medical director citing the highest range verified in the procedure is sufficient. If patient results are higher than the material used to verify the AMR but less than the AMR, they can be reported as they are. For example: AMR = 0–1,000 ng/dL but material available only up to 700 ng/dL; results between 700 and 1,000 ng/dL can be reported.

- In many cases, the manufacturer will have verified extended ranges beyond the AMR using recommended manual or autodilution/concentration protocols. In this situation, reporting of results up to those limits is also acceptable after the AMR has been verified (CHM.13710). This range reflects the reportable range verified by the manufacturer.
- Results greater than the AMR or range verified by the manufacturer should be reported using the "greater than" symbol.
- In situations where the desired results are greater than the AMR or range verified by the manufacturer (dilution to endpoint), CHM.13720 in the CAP checklist requires the laboratory director to specify and document what the maximum dilutions are on an analyte-by-analyte basis. This will require dilution studies to confirm result linearity in this range.

  There is no such thing as an "absurd" or "invalid" endpoint/maximum allowable dilution value. There is only validated and nonvalidated dilution. It is up to the laboratory director in conjunction with the clinical staff and vendor to determine what the maximum dilutions will be. For example, it is not unreasonable for creatine kinase to be "diluted to endpoint" because in extreme rhabdomyolysis CK values greater than the AMR should be reported to monitor response to treatment. This can also be applied to many tumor markers for the same reason.

1. College of American Pathologists. CHM.13600 AMR verification. In: Chemistry and toxicology checklist. April 2014:15.
2. College of American Pathologists. CHM.13710 Diluted or concentrated samples. In: Chemistry and toxicology checklist. April 2014:15.
3. College of American Pathologists. CHM.13720 Maximum dilution. In: Chemistry and toxicology checklist. April 2014:16.

David N. Alter, MD, DABCC
Clinical/Chemical Pathologist
Blood Bank Medical Director
Clinical Professor of Pathology
College of Human Medicine
Michigan State University
Spectrum Health Regional Laboratory
Grand Rapids, Mich.
Vice Chair, CAP Chemistry Resource Committee