Health Literacy Assessment via STOFHLA: Paper vs Computer Administration

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Abstract

Background. Low health literacy affects more than one-third of American adults, resulting in poor physician-patient communication, worse health outcomes, and increased medical costs. Many physicians are uninformed of their patients' health literacy status. Current paper-based surveys require extra staff, time, and resources for administration, while a computer-based survey may provide efficient assessment to increase provider awareness. The study assessed the efficacy of a computer-based health literacy test compared to an established, paper-based format for use in an office setting.

Methods. A prospective, non-blinded, randomized experimental design was conducted. A brief demographic survey and health literacy test (STOFHLA) was administered to 100 adult subjects at a Midwestern family medicine residency clinic. Recruitment flyers were distributed in the office and all eligible, willing patients were randomized to one of two groups. Fifty participants were administered the paper test and 50 were administered the computer-based test.

Results. The majority of subjects had "adequate" health literacy (85%) and completed the test within the allotted time period (82%). When comparing the paper and computer groups, there were no statistically significant differences for demographics, test scores, or completion time.

Conclusions. A computer-based health literacy test is as effective as an established, paper-based format to assess health literacy in a family medicine office population. Future research studies should investigate the impact of having patient health literacy scores available to the physician prior to the office visit and how it may affect communication, compliance, and health outcomes.
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Introduction

Health literacy is an important factor in medicine that has been associated with patient-physician communication, health outcomes, and costs.[1,2] According to Healthy People 2010, health literacy is the "degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions and follow instructions for treatment."[3] Health literacy is one of the strongest predictors of health status, surpassing education level, income, and ethnicity.[4]

More than one-third of American adults have marginal health literacy and suffer significant consequences.[3] Low health literacy is associated independently with poor health outcomes.[1,4] In one study, 33% of diabetic patients with adequate literacy had good control of hemoglobin levels ($HgA_{1c} \leq 7.2\%$) compared to only 20% of low-literacy patients.[5] Another study found that Medicare patients were 29% more likely to be hospitalized if they had low health literacy.[6] Patients with inadequate health literacy were subject to increased

medication errors, missed appointments, and decreased access to health care.[7] Inadequate health literacy costs an estimated $73 billion dollars in extra health care services.[8] Furthermore, poor patient-physician communication associated with low health literacy may lead to increased malpractice suits.[4]

Despite these consequences, most health care providers are unaware of their patients' health literacy status. While low-health literacy was associated with identifiable risk factors such as increased age, limited education, and certain ethnic minorities, providers do not predict health literacy skills reliably based on demographic factors or appearance alone.[9,10] Further, patients are unlikely to admit their low-literacy status or lack of comprehension to health care providers.[10]

Finally, low health literacy affects all segments of the population.[10] For these reasons, providers should use a "universal precautions" approach with all patients.[1,3,11] However, providers may have limited time during clinical encounters to use tools which improve communication with low health literate patients. Thus, health literacy assessment could potentially identify patients who require extra time and resources for improved communication and patient care.[4]

Numerous instruments for testing health literacy have been validated and typically are administered verbally.[5] For example, the Rapid Estimate of Adult Literacy in Medicine (REALM)[12] and the Test of Functional Health Literacy in Adults (TOFHLA)[13] involve scoring patients' pronunciation of medical words. The Newest Vital Sign[14] evaluates patients' ability to understand a nutrition label. The Short Test of Functional Health Literacy in Adults (STOFHLA) uses fill-in-the-blank passages taken from medical instructions that patients might encounter, and takes seven minutes to administer. The STOFHLA has been validated, and demonstrated comparable results to the REALM and TOFHLA.[6]

Currently, most health literacy assessment tools are administered via a paper-based format.[6,15,16] Little is known about using a timed, computer-based test. A computer format may be more cost-effective and efficient for practices to implement, especially if integrated into web-based check-in systems and electronic medical records.

This study's objective was to evaluate if a paper-based assessment tool can be utilized in a computer format and provide comparable results, thus providing the basis for further validating the tool's use through computer administration. The STOFHLA was chosen for this study due to its convenience, the structure of the assessment as a viable option for a computer administration, and its ability to administer via computer without audio assistance devices.

Methods

A brief demographics survey and the STOFHLA were administered to 100 adult subjects at a Midwestern family medicine residency clinic. The study was approved by two local Institutional Review Boards.

Subject selection criteria and sample size justification. Adult patients or parents of child patients were asked to participate in this study when checking-in for a scheduled medical appointment. The eligibility criteria for participation in this study included: (1) English-speaking, (2) adult ($\geq$ 18 years of age), (3) able to use a computer, and (4) able to provide informed consent. One hundred surveys were needed to achieve 90% power. Approximately 525 patients were seen at the clinical site each week.

Recruitment. A recruitment information sheet about the research was provided to all

eligible participants when they checked-in for their scheduled appointment. The Flesch-Kincaid[17] readability of recruitment fliers was at the 7.1 grade level. Those who agreed to participate met with one of the investigators to learn more about the study, its requirements, and eligibility. Each willing participant signed an informed consent form.

The session included a survey for demographics and technology use, followed by the timed (7 minute) Short Test of Functional Health Literacy in Adults.[12] Technology experience was scored on a scale of 1-6, with one equal to low experience and six equal to high experience. Technology self-efficacy was assessed as a composite score from four statements; the minimum score was 5 and maximum score 20. Subjects were randomized to receive the test either via a computer-based system or a paper form. Fifty subjects received each type of test format.

Study instructions were read to each participant by one of the investigators. The standard STOFHLA was transferred to a digital format and delivered via a laptop for the computer group. The computer version was designed to resemble the test format (i.e., instructions and number of questions) and layout of questions (i.e., sentences and corresponding word-choice options) of the paper version. Administration of the STOFHLA for both groups was conducted using standard procedure, scoring, and interpretation (see Table 1). All participants received a $15 gift card upon their study completion.

Data analysis procedures. Data were managed using the Statistical Package for the Social Sciences (SPSS version 17.0; Chicago, IL). Descriptive statistics were tabulated. Univariate comparisons between subgroups of participants used Pearson's chi-square for categorical variables (with Fisher's correction if needed). For continuous variables, independent samples t-tests or ANOVA were used to compare non-skewed variables or Mann Whitney or Kruskal Wallis tests for non-normal distributions. All statistical tests were two-tailed and alpha was set at 0.05.

Table 1. Interpretation of the STOFHLA raw scores.*

Raw score	Interpretation
0-16	Inadequate: may be unable to read and interpret health texts
17-22	Marginal: has difficulty reading and interpreting health texts
23-36	Adequate: can read and interpret most health texts

*Adopted from Barber et al.[18]

Results

One hundred participants from a single family medicine residency clinic completed the study. Subjects were primarily female (82%), white (62%), and had an annual household income less than $20,000 (72%). The age distribution of participants was: 27%, 21-30 years old; 17%, 31-40 years old; 21%, 41-50 years old, and 24%, 51 years old and older. Participants who were married, never married, or not now married were

distributed evenly (33.7%, 32.7%, and 33.7% respectively). Most participants had either high school graduation equivalence (37%) or attended college for less than 4 years (35%).

Thirty percent of participants described themselves as "up-to-date with technology". The next most common descriptors (19% each) were: "I don't have time to keep up with the latest technology" and "I immerse myself in technology as a hobby". When asked about their experience with technology, the majority reported using computers (69%) and cellular/mobile phones (83%) on a daily basis. The majority "agreed" or "strongly agreed" that they were: comfortable using a computer on their own (77%), confident in their abilities to use most technological devices (80%), and self-sufficient using a new technology after only a short training (80%). Technology self-efficacy and experience did not differ between computer and paper groups (Table 2).

The majority of subjects completed the STOFHLA within the 7-minute time (82%). The median score on the health literacy test was 33 (mean = 30.97, SD = 6.21, range = 10-36). The individual's functional health literacy score on the test was interpreted as being in one of three levels (see Table 1). The majority of the participants were rated as having "adequate" health literacy (85%); 11% were "marginal" and 4% were "inadequate". The characteristics of the two groups are displayed in Table 2. The two groups did not differ statistically by race, age group, education level, employment, or income level.

For the computer and paper test administrations, the majority of subjects had adequate health literacy (86% and 84% respectively). Twelve percent of participants in the computer group had marginal health literacy compared to 10% of the participants in the paper group. Those with inadequate health literacy were at 2% and 6%, respectively. STOFHLA scores did not differ significantly between paper (mean = 31.0, SD = 6.77) and computer (mean = 30.9, SD = 5.67) groups ($t(98) = 0.48$, $p = 0.96$; Table 3). For both computer and paper administration, the majority of people (84% and 80% respectively) completed the STOFHLA within the allotted 7-minute testing period, and there was no significant difference between groups, χ^2 (1, N = 100) = 0.27, p = 0.60.

Finally, the participants' comfort level with using computers did not impact their health literacy score significantly based on which type of test they were administered ("comfortable", paper version, mean = 31.8, SD = 6.28, "comfortable", computer version, mean = 31.9, SD = 4.67, t(66) = -0.088, p = 0.93; "uncomfortable", paper version, mean = 25.67, SD = 8.64; "uncomfortable", computer version, mean = 25.00, SD = 3.61, t(7) = 0.651, p = 0.53).

Discussion

Health literacy is a significant indicator of health status, and assessment has the potential to enhance patient care. Busy schedules and limited appointment times call for an efficient assessment tool. Implementing a computer-based test may be more cost-effective and efficient than a paper-based method for incorporation into an office practice. A computer-based survey could be completed prior to an office visit, such as at a computer in the office waiting room or at home through a web-based check-in service.

In the advent of electronic medical records systems, a computer-based survey could be integrated into the flow of the office system and recorded in the patient's electronic medical chart. Depending on the implementation strategy chosen, initial costs may include the purchase of a dedicated computer or kiosk. Administering this

Table 2. Demographic comparisons for paper vs. computer groups.

DEMOGRAPHICS	**Paper (n=50)**	**Computer (n=50)**	Test	df	p-value
	%	%	χ^2		
RACE					
White	73%	54%	3.771	1	.052
Non-white	27%	46%			
AGE GROUP					
18-20 years old	8%	14%			
21-30 years old	22%	32%	7.631	4	.106
31-40 years old	20%	14%			
41-50 years old	16%	26%			
51+ years old	34%	14%			
EDUCATION					
Less than High School or GED	16%	16%			
Grade 12 or GED	42%	32%	4.323	3	.229
College 1-3 Years	26%	44%			
College 4+ Years	16%	8%			
EMPLOYMENT					
Not working	66%	54%	1.500	1	.221
Working	34%	46%			
INCOME					
Less than $20,000	76%	68%	.794	1	.373
Greater than $20,000	24%	32%			
	Mean (SD)	Mean (SD)	t	df	P-value
TECHNOLOGY EXPERIENCE	1.75 (.85)	1.84 (.93)	-.56	98	.577
TECHNOLOGY SELF-EFFICACY	19.5 (3.7)	19.4 (2.9)	.073	91	.942

Table 3. Health literacy outcome comparisons for STOFHLA paper vs. computer.

STOFHLA OUTCOMES	**Paper (n=50)**	**Computer (n=50)**	Test	df	P- value
	%	%	χ^2		
COMPLETED IN 7 MINUTES					
Yes	80%	84%	.271	1	.603
No	20%	16%			
STOFHLA SCORE CATEGORY					
Inadequate	6%	2%	1.103	2	.576
Marginal	10%	12%			
Adequate	84%	86%			
	MEAN (SD)	MEAN (SD)	t	df	P-value
STOFHLA SCORE	31.0 (6.8)	30.9 (5.7)	.048	98	.962

computer-based test may not require additional dedicated personnel or on-going resources, which could decrease its cost compared to a paper-administered version.

This study demonstrated that a computer-based health literacy test was comparable to the paper-based form in the study setting. The two groups were similar in health literacy score and time required to complete the survey. Moreover, there were no differences in demographics to confound the results and both groups had similar technology experience and self-efficacy scores. In the overall study sample, slightly less than a quarter of participants did not feel comfortable using computers. Those patients may need occasional assistance with computerized testing until their confidence and comfort levels improve. These findings suggested that a computer-based STOFHLA test could be used in an office setting to assess patients' health literacy accurately.

Unfortunately, many health care providers are unaware of their patients' health literacy status. As previously noted, low health literacy was associated with decreased access to medical services and poor health outcomes. Increasing provider awareness of their patients' understanding of health concepts may improve communication, health care access, and overall health outcomes.

Limitations. This study population was limited to a single clinical site in a Midwestern location. The sample size was low, as is typical in preliminary studies involving the testing of technology as an application for assessing patient skills and knowledge. The results of the health literacy rates may not be representative of the overall population. Although the type of test administered (paper-based or computer-based) was randomized, participant selection was not randomized. The results may be generalizable only to tests using desktop or laptop computers, and not to other technology such as kiosks or touch screens. These variations provide an area of future research.

Conclusions

A short, computer-based test is an accurate method to assess health literacy in a family medicine office population. Previous studies have revealed the link between low health literacy and poor health status. Future research studies need to be conducted to assess the implementation of a computer-based health literacy assessment and its effect on patient care. There is a need to investigate the impact of having patient literacy scores available to the physician prior to the office visit and how it may affect physician-patient communication, medication compliance, and long-term health outcomes within the patient-centered medical home.

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Are Medical Students Able and Willing to Edit Wikipedia to Learn Components of Evidence-Based Practice?

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Abstract

Objective. This study sought to measure the ability and receptiveness of medical students for creating evidence-based edits in Wikipedia for learning components of evidence-based practice.
Methods. Senior medical school students in an elective in clinical informatics and evidence-based medicine during 2007 (n=21) or 2008 (n=18) were taught how to place succinct summaries of studies in Wikipedia. Online help was provided. In 2008, an online template facilitated editing.
Results. Combining the two years, all students but one (97%) cited articles in PubMed and 85% created links to abstracts in PubMed. Most students (79%) reported a study design and 72% provided numeric results. In 2007, 14% of students created complete citations, compared to 78% in the second year ($p < 0.05$). At two months follow-up, 44% of students had at least one edit improved and one edit from 2007 was deleted. In 2007, 83% (15/18) of the students agreed or strongly agreed that the exercise should be offered to the next year's class. In 2008, this rate was 100% (16 respondents).
Conclusions. Among these self-selected students, most students were positive about the assignment and almost all created edits that succinctly summarized research results and attributed evidence.
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Introduction

Many physicians have difficulty reading and interpreting medical research.[1-3] More specifically, physicians have difficulty interpreting probabilistic results,[4-6] may overgeneralize findings to incorrect populations,[7-9] and may carry details incorrectly from studies into clinical practice.[3,7,8,10,11] Adverse clinical outcomes have been documented that may arise from these difficulties in interpreting and applying research evidence.[8,9] In summary, when physicians try to answer questions, they are almost as likely to make an incorrect conclusion as a correct conclusion.[12] This may place physicians in the "position of knowing less than has been proved".[13]

Teaching evidence-based practice and critical appraisal is challenging as exemplified in a recent negative result of a randomized controlled trial of a carefully designed course for residents in internal medicine.[14] Performing clinical research in residency may increase critical appraisal skills,[15,16] but insufficient time hinders research.[17] Writing critically appraised topics (CATs) is easier than performing research.[18] CATs begin with a clinical question, usually based on a specific patient encounter, then summarize the best clinical

evidence. However, drawbacks to CATs include the difficulty in keeping them up-to-date as new research emerges, and difficulties in sharing CATs across institutions.[19] A Catmaker can help create CATS;[20] a CAT Crawler can help locate CATs;[21] a network of CATs may help distribution;[22] and new collaborative editing tools such as Wikis provide logical solutions to the distribution and maintaining currency of clinical knowledge gained from participating projects.

A simpler approach might involve the use of Wikis to teach components of evidence-based practice. While use of Wikis has been encouraged in medical education[23-27] and teaching public policy,[28] there appears to be no published research on the acceptance of their use for this purpose. This paper reports observations from the introduction of collaborative editing of Wikipedia into the curriculum of a senior medical school elective.

Methods

During March 2007 and 2008, senior medical students at the University of Texas Health Science Center at San Antonio chose an elective that was advertised as being for "students who want to master information". The elective included 4 hours of classroom time for learning about Wikis and additional online instruction was available. For the 2008 class, an online template for edits was developed for student use.

Students were encouraged to make two edits in Wikipedia for a biomedical topic of their choice: One edit was to address the diagnosis while the second edit was to address treatment of their topic. The students were instructed to search for a *representative* original study for each edit with the goal of succinctly summarizing the type of study and its central finding. More specific instructions are summarized in Table 1.

At the end of the last session, the students were asked to complete an, anonymous survey (Table 2). The survey asked three questions about editing Wikipedia using a five-item Likert response and also asked for open ended comments. The pages and their histories at Wikipedia were reviewed systematically after two months for the criteria listed in Table 3.

The Institutional Review Board determined that this research did not involve human subjects and that Code of Federal Regulations (45 CFR 46) did not apply.

Table 1. Instructions given to students.

Instructions given only in 2007
• Succinctly summarize the type of study and its central finding in one sentence.
Instructions given only in 2008
• Use the online template to help you design a short summary.
Instructions given both years
• Note the authorship of the study if by a well-recognized evidence-based group such as the Cochrane Collaboration or United States Preventive Service Task Force.
• Numerically represent the results if possible.
• Link concepts in their edit to more detailed pages at Wikipedia and elsewhere. For example, students were given a list of instructions on linking to Wikipedia pages about randomized controlled trials, sensitivity, and number needed to treat.
• Link the edit to the citation at PubMed.
• Place the edit in the relevant section of the resource they choose to edit.
• Avoid making a clinical recommendation unless they truly feel expert on a topic.

Table 2. Anonymous survey at course end.

1. Should this exercise be repeated for next year's class? 2. Do you think you will make medical edits to a collaborative-edit system such as Wikipedia in the future? 3. Would you be more likely to make medical edits in the future if the interface for editing were easier to use?
The responses allowed for each question were: Strongly disagree, Disagree, Neither agree nor disagree, Agree, Strongly agree

Table 3. Review of edits after two months.

Review of the original edits a. A statement of a study design. b. Numeracy by stating either sensitivity and specificity or a measure of risk reduction. c. A hyperlink to the PubMed citation. d. A complete citation according to Wikipedia standards. e. A hyperlink to related content in the Wiki. Review of the page history at two months a. Changes or deletions of the original edits. b. Changes to any part of the page containing the original edit to correct vandalism.

Results

Compliance with the assignment. All students complied with the assignment; however, one student in 2008 cited recommendations from UpToDate (a subscription-based clinical reference tool) rather than original research. In 2007, 21 students edited 23 pages. In 2008, 18 students edited 21 pages. One student in 2007 created a new Wikipedia page.

Content of edits. Combing the two years, all students but one (97%) cited articles at PubMed. Most students (79%) reported a study design and 72% provided numeric results (Table 4). Regarding hyperlinking edits to underlying sources, 85% of students created hyperlinks to abstracts at PubMed. In 2007, only 14% created a formal citation, whereas 78% of students in 2007 created a formal citation ($p < 0.05$). Most of the students (79%) created additional hyperlinks to a relevant web page either within or outside of Wikipedia. Almost half (44%) of students contributed their edits anonymously. Of the 56% of students registered at Wikipedia, none provided their real names.

An example of an exemplary edit from 2007, that is still present in 2011, is on the page "Bowel Obstruction":[*]

> "According to a meta-analysis of prospective studies by the Cochrane Collaboration, the appearance of water-soluble contrast in the cecum on an abdominal radiograph within 24 hours of oral administration predicts resolution of an adhesive small bowel obstruction with a pooled sensitivity of 96% and specificity of 96%."[**]

[*] Available at: http://en.wikipedia.org/wiki/Bowel_obstruction.

[**] The edit can be viewed in isolation in the page history at Wikipedia: http://en.wikipedia.org/w/ index.php?title= Bowel_obstruction&action=historysubmit&diff=119060338&oldid=117779804.

An exemplary edit from 2008, which used the online template for the class to add an edit to the page "Cervical Cancer" and is present in 2011 after being moved to the page Cervical Screening:[†]

> "HPV testing can reduce the incidence of grade 2 or 3 cervical intraepithelial neoplasia or cervical cancer detected by subsequent screening tests among women 32-38 years old according to a randomized controlled trial. The relative risk reduction was 41.3%. For patients at similar risk to those in this study (63.0% had CIN 2-3 or cancer), this leads to an absolute risk reduction of 26%. 3.8 patients must be treated for one to benefit (number needed to treat = 3.8)."[‡]

Receptiveness survey at course end. In 2007, 83% of students agreed or strongly agreed that the exercise should repeat next year (Table 4). Most (72%) said they would be more likely to make future edits if editing was technically easier. In 2008, all respondents to the survey agreed or strongly agreed that the exercise should repeat the next year. Selected comments are in Table 5.

Table 4. Results.

	Year		Combined
	2007	**2008**	
	N=21	N=18	N=39
Registered at Wikipedia	52%	61%	56%
Quality of edits			
Study design stated	76%	83%	79%
Numeracy provided	72%	72%	72%
Hyperlink to PubMed abstract	90%	78%	85%
Complete citation	14%	78%*	
Hyperlinks to other web pages	76%	83%	79%
Durability of edits at 2 months			
Improved	48%	44%	46%
Hosting pages vandalized	67%	56%	62%
Receptiveness survey	N=18	N=16	N=34
Should the project continue next year?	83%	100%	91%
Plan to do future edits?	72%	69%	71%

Notes: Quality outcomes were scored as present if at least one of a student's edits contained the outcome.
* $p < 0.05$ by Fisher's exact test.

[†] Available at: http://en.wikipedia.org/wiki/Cervical_screening.
[‡] This edit can be viewed in isolation in the page history (http://en.wikipedia.org/w/ index.php?title=Cervical_ cancer&action=historysubmit&diff=198849853&oldid=197483778)

Table 5. Selected comments.

2007
The following are 4 of the 9 comments. The last comment was the only negative comment received. • "I think the current system is not very difficult, especially after seeing how to do it in class. Without this project, I might never have tried to edit Wikipedia. Now, I think that when I look up the answer to something, I might just throw the answer up for others who wonder the same thing." • "Learning how to edit Wikipedia was a fun exercise, I don't know if I will do it again in the future." • "Have used Wikipedia before, but did not realize that that the general public can write info in it." • "I was forced into this course by the registars [sic] office. I hope the next class will not have to take this course. It did not help me."
2008
The following are 3 of the 13 comments. There were no negative comments. • "The actual editing of a Wiki page is not necessarily something I would do in the future, but the process of learning how to do good research and cite articles for evidence-based documents was very helpful." • "The Wiki edit was useful and I think I will look at the medical edits in the future because of this class." • "This was a good learning experience....never knew how Wiki worked before."

Status of edits at two months. At two-months follow-up, 46% of students had at least one edit improved and one edit from 2007 was deleted (Table 2). After the original edits were completed, one improvement occurred within three minutes and one within four hours. One student who completed her edits over several days had one of her earlier edits improved upon amid her work. Most of the improvements were corrections of typographical errors and improvements in formatting. Some of these edits were made by automated bots at Wikipedia (http://en.wikipedia.org/wiki/Wikipedia:Bots). One improvement was added by the original student and is the only instance of a student returning to Wikipedia after the course ended. The pages edited by 62% of students had additional edits in response to incidental vandalism to the pages, but in no instance was the vandalism done to an edit by a student.

Discussion

This study showed that a selected group of senior medical students can make short edits to Wikipedia and are sufficiently receptive to the assignment to recommend the assignment be repeated the next academic year. The provision of an online template may have helped the technical quality of the edits.

This participatory method of learning is consistent with active learning[29] as opposed to learning via lecture and rote memorization.[30] Our assignment is similar to collaborative writing of a letter to the editor.[31]

Although this project focused on learning evidence based practice rather than how to contribute to Wikis, some students may benefit from learning how to edit Wikis because of their future work. Students who become clinical informationists may edit Wikis as hospitals are starting to use Web 2.0 methods such as Wikis to codify their institutional knowledge.[32] Students who become researchers may edit Wikis as a way to share knowledge for team science.[33-36]

There are limitations to this study. First, this was an uncontrolled study in a small group of selected senior medical students. Second, this study did not measure whether the students actually learned evidence-based practice or altered their learning habits. Third, this project did not have the resources to examine formally whether the edits correctly summarized the article. Accuracy was sought by encouraging the students to work in pairs and having a faculty internist review each edit. We note that ensuring correctness is a limitation of any participatory learning. In comparison to CATs, however, Wikis can be corrected and maintained much easier. Lastly, the optimal structure of a medical edit is not known. For example, should the edit state the study design or is a link to the abstract adequate?

This study showed that teaching components of evidence-based practice with collaborative editing is feasible in limited group of self-selected medical students. Further study is needed in a broader group of students. In addition, research can be conducted in other Wikis that may emerge and become more scholarly than Wikipedia. If a broader group of students is receptive, then research can address whether editing a Wiki improves the knowledge, skills, and behavior of medical students regarding evidence based medicine.

> *"A doctor who accesses the world wide web … to seek the answer to a question but does not find it there and has the facility to place material on the web … must place that answer on the web where the next one to ask the same question can find it".*[37]

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Keywords: evidence based practice, medical education, medical informatics

Primary Angiitis of CNS: A Diagnostic Dilemma

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Introduction

Primary angiitis of the central nervous system (PACNS) is a rare disease of unknown etiology.[1] It is a serious type of vasculitis that not only affects CNS vessels in the absence of systemic inflammatory diseases,[2] but potentially causes neurological deficits in less than 40% of patients.[3] Persistent unexplained headaches and altered mental status are the most common presenting symptoms with PACNS. It is more common in males than females with the presenting age in the 5th decade of life. Magnetic resonance imaging (MRI), cerebrospinal fluid, and cerebral angiograms are found to be abnormal, but non-specific. Brain biopsy is performed, not only to establish diagnosis, but for planning the management.

Case Report

A 42-year-old female, known to have migraine headaches, presented with a history of occipital headaches and neck stiffness of a few hours duration. She took acetaminophen and oxycodone for pain without relief. While driving, she felt dizzy and nauseated. She later had six episodes of vomiting. She developed generalized weakness to the point that she could not stand. She has no history of falls.

The physical examination, including the neurological examination, was normal. It was unclear if any neurological deficits, that might prevent her from standing, resolved or if the complaints of generalized weakness were subjective. Initial evaluation including lumbar puncture and MRI revealed moderate cervical stenosis without any acute pathology and some occipital edema, thought to be attributed to migraine. The patient was given analgesics and her symptoms improved. She was discharged on day four of hospitalization with a diagnosis of complicated migraine.

Eight days later, the patient again presented with intractable headache, weakness of lower extremities, and photophobia. Her neurological examination revealed diminished motor strength 4/5 in all four extremities. An MRI on admission revealed leptomeningeal enhancement over the cerebral hemispheres. A lumbar puncture showed no evidence of any infectious process. Cerebrospinal fluid (CSF) analysis revealed protein at 51 mg/dL, glucose at 55 mg/dL, white blood cells at 9 cells/µL, lymphocytes at 42%, and neutrophils at 47%. HIV, Lyme's disease, tularemia, syphilis, *Bartonella hansellae*, mycoplasma, *Coxiella burnetti*, and West Nile virus serologies were normal. ANA, C-ANCA, and P-ANCA were negative.

The patient was given analgesics with minimal relief. On day 4 of this hospital admission, the nature of her headache changed from occipital to spinal. On day 5, she developed left upper extremity weakness.

MRI was repeated and showed ischemia in the right paracentral lobule. A magnetic resonance angiogram (MRA) revealed multiple short segment areas of stenosis with normal intervening segments throughout the bilateral middle, anterior, and posterior cerebral arteries, suggestive of vasculopathy. These findings were verified by arteriogram. Later, her weakness evolved from left to right upper extremity and she developed slurred speech.

The patient was started on IV methylprednisolone. After a few days of steroid therapy, her speech improved with residual weakness in her right upper extremity. A brain biopsy was performed from the occipital region and samples were taken from dura, cortex and white matter. After stabilizing her condition, she was sent home with tapering steroids. Biopsy results later showed mild gliosis.

Discussion

Diagnostic criteria of primary angitis of CNS were proposed in 1988 by Calabrese and Mallek.[4] Those criteria included: (a) an unexplained neurologic deficit despite aggressive diagnostic workup, (b) a high-suspicion angiogram for arteritis and/or histopathological evidence of arteritis limited to the CNS, and (c) no evidence of systemic vasculitis or exclusion of all those disorders capable of mimicking with vascular inflammation of the CNS.

Reversible cerebral vasospastic syndrome (RVCS) is the most important and most common clinical mimic of PACNS.[5] Early differentiation between the two is critical since the management for PACNS may require cytotoxic agents.[6] Headache, encephalopathy, and focal neurological deficit are found commonly in PACNS. Non-specificity of symptoms and their subtle progression result in extended duration between symptom onset and diagnosis. In contrast, patients with RVCS present with severe headaches of sudden onset and focal neurological symptoms. Typically, RVCS patients initially undergo a more intense diagnostic evaluation with a shorter time between onset of symptoms and ultimate diagnosis.[7]

CSF analysis is abnormal in 80% to 90% of patients with true PACNS, though it is usually normal in RVCS. CSF samples of patients with PACNS may show only modest elevations in white blood cell count and total protein level.[3]

MRI is abnormal in 90% to 100% of patients.[8] Infarcts may be seen in approximately 50% of cases. When present, infarcts are usually seen bilaterally in multiple-vessel tributaries, as mass lesion, ischemic demyelination, or cortical necrosis.[3] In contrast to this, MRI is normal in the vast majority of patients with RCVS.[9]

CNS angiogram has limited sensitivity for detecting vasculitis.[10] A range of noninflammatory vasculopathies can cause angiographic findings similar to those seen with PACNS. Therefore high pretest probability plays a major role in supporting the angiographic findings, which range from normal to areas of regular or irregular vascular luminal abnormalities. Although the initial findings may be similar as of PACNS, the most specific finding of RCVS on angiogram is the reversibility of vascular abnormalities over the period of time.

Cerebral biopsy is required for accurate diagnosis of PACNS and starting prolonged immuno-suppressive treatment.[11] Vasculitis affects vessels in a skipped and segmental pattern. The sensitivity of brain biopsy may be less than 50%.[7] PACNS usually runs a progressive and fatal course if left untreated. High doses of corticosteroids and cyclophosphamide are the mainstay of treatment. RVCS, on the other hand, is treated with a short course of glucocorticoids and nifedipine, which typically results in complete radiological recovery.[12]

Differentiation of PACNS from RCVS is a diagnostic dilemma due to lack of any specific criteria to differentiate between the two (see Table 1). Since PACNS follows a more severe course, early administration of immuno-suppressive agents is required to reduce mortality and morbidity. On the other hand, RCVS cases simply can be observed or treated with corticosteroids and calcium channel blockers. Therefore, physicians should avoid treating patients with RCVS unnecessarily with immunosuppressive agents. Misdiagnosing PACNS patients with RCVS can prove fatal. Further research is needed to clarify grey areas.

Table 1. Characteristics of PACNS and RVCS.*

	PACNS	RVCS
Gender Predominance	Men > Women	Women > Men
Median Age at Presentation	40-60 years	20-40 years
Presentation	Chronically progressive headaches	Acute and severe headaches
Focal Symptoms Neurological Symptoms	Yes, but rare at onset of headache	Yes, may occur with onset
CSF Findings	Leukocytosis and elevated total protein level, mild to moderate	Normal
Treatment	Prednisone with cytotoxic agent	Prednisone with calcium channel blocker

*Table adapted from Birnbaum and Hellmann.[7]

Conclusion

The most important clinical mimic of PACNS is RCVS. Both diseases follow different courses with PACNS being fatal as compared to the more benign and reversible course of RCVS. Early administration of immunosuppressive agents has significant impact on the prognosis of PACNS. Early differentiation is important to avoid adverse outcomes.

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Key words: primary angiitis of the central nervous system, diagnosis, case report

Spontaneously Sealed Aortic Dissection Presenting with Multiple Ischemic Strokes

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Introduction

Aortic dissection is a rare and potentially fatal disease. It usually presents with severe chest pain radiating to the back, isolated back pain, or abdominal pain.[1] Atypical symptoms such as dizziness, vertigo, syncope, weakness or numbness are uncommon. The prevalence of neurologic symptoms in aortic dissection account for up to 42% of cases.[2] One study revealed that 29% of patients with type A aortic dissection presented with neurologic manifestations, but only two-thirds of these patients reported chest pain.[3] Based on these percentages, approximately 10% of patients present with neurologic symptoms and without chest pain. Neurologic manifestation in aortic dissection included ischemic stroke (16%), ischemic neuropathy (11%), syncope (6%), seizures (3%), hypoxic encephalopathy (2%), and spinal cord ischemia (1%).[3]

Case Report

A 21-year-old Caucasian male was transferred to our facility for workup of acute ischemic stroke. He was playing a video game when he suddenly felt a severe headache followed by diplopia, vomiting, confusion, and generalized weakness. He had no relevant past medical history. His family history was unremarkable for atherosclerotic or thromboembolic diseases.

The patient's cardiovascular examination was normal. He had no carotid bruit. He was lethargic and confused. There was evidence of left-sided weakness, although a complete neurologic examination was limited by the decreased level of consciousness.

A CT scan showed an acute ischemic infarct involving the right temporal lobe. An MRI of the brain with contrast revealed an ischemic infarct involving the right occipital lobe and the posterior aspect of the right temporal lobe. Another infarct involved the left superior cerebellum. (See Figures 1 and 2.) A hypercoagulable workup on admission revealed positive antiphospholipid antibodies.

Given the presence of multiple strokes in different vascular territories, a cardioembolic phenomenon was suspected and the patient underwent a transesophageal echocardiography (TEE). The TEE was negative for cardiac emboli. However, it revealed the presence of a small dissection flap in the ascending aorta (Figure 3) and thickening of the intima of the descending aorta (Figure 4). These findings suggested an aortic dissection with a dissecting channel that healed spontaneously and left a small flap in the ascending aorta. An MRA of the head and neck was negative for aneurysm, dissection, or stenosis. A CTA of the chest showed no evidence of dissection or other abnormalities. The TEE was repeated one week later, as a preoperative workup for surgical repair of the dissection, and showed a complete resolution

of the dissection flap and decreased prominence of the intimal thickening in the descending aorta.

Surgery was deferred and the patient was treated conservatively with blood pressure control, physical therapy, and anticoagulation for possible antiphospholipid syndrome. He improved progressively and was discharged home to continue physical therapy. In a 6-month follow-up exam, he showed no evidence of neurologic deficit on the physical examination. The TEE was negative. The antiphospholipid antibodies were normal indicating a false positive test initially. The diagnosis of antiphospholipid syndrome was unlikely because of the repeated negative antiphospholipid antibodies test and the absence of family history of hypercoagulability. Thus, anticoagulation was stopped and the embolic strokes were assumed to be secondary to the aortic dissection.

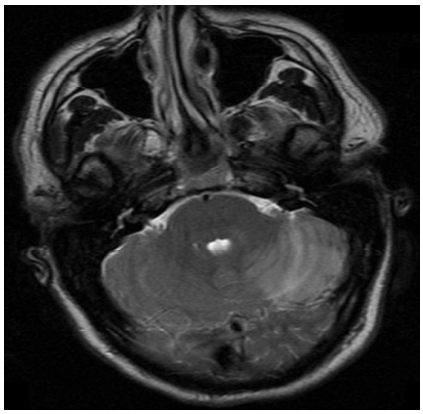

Figure 1. A T2 weighted MRI indicated an acute ischemic infarct involving the left superior cerebellum in the region of the left superior cerebellar artery.

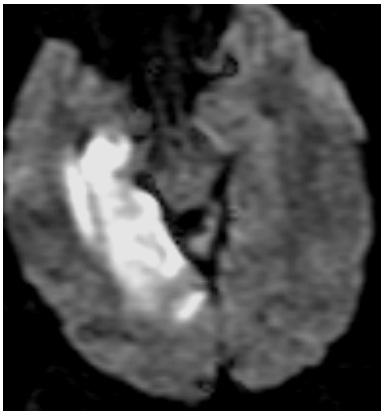

Figure 2. A diffusion weighted image showed acute ischemic infarcts of the right occipital and the posterior aspect of the right temporal lobe in the region of the right posterior cerebellar artery.

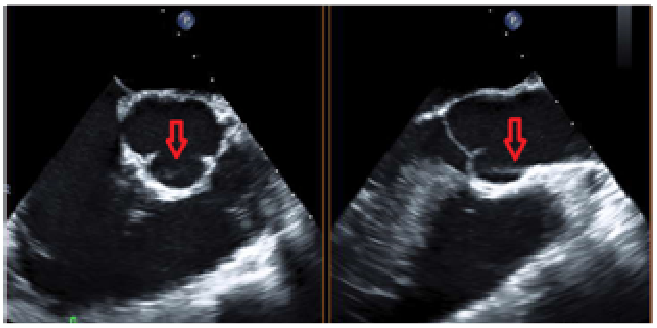

Figure 3. Two views of the ascending aorta on the trans-esophageal echocardiogram show the intimal flap just above the aortic valve (red arrows).

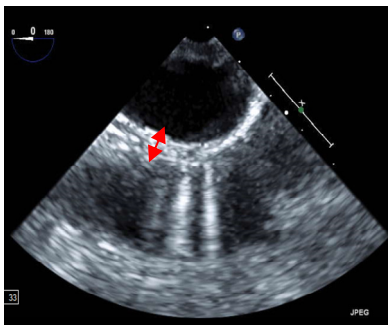

Figure 4. Intimal thickening of the descending aorta appears to represent, in the setting of the dissection flap in the ascending aorta, an aortic dissection that has sealed and healed spontaneously.

Conclusion

Cerebral infarcts in patients with aortic dissection are due to common carotid occlusion by progression of the false lumen with subsequent thrombosis or by intimal detachment.[4] Another possible mechanism is an artery-to-artery embolism from a thrombus developed on the intimal surface of the dissected artery. It is difficult to know which mechanism is involved without an autopsy. In our case, the most likely mechanism was embolization, since there was no evidence of dissection in the carotids or cerebral arteries on the imaging. On the other hand, it is unusual for the dissection flap to follow two different pathways: the right posterior cerebral artery and the left superior cerebellar artery. These were the arteries corresponding to the vascular territories of the ischemic strokes in our patient.

The natural pathophysiology of aortic dissection involves the development of an intima-medial tear. The tear could be limited (incomplete dissection) or progress to form a dissecting channel and subsequently an aneurysm or rupture of the aorta.[5] Spontaneous healing of aortic dissection is very rare. The mechanism of spontaneous healing of aortic dissection involves clotting of the hematoma followed by fibrosis. Another possible mechanism is endothelialization and obliteration of the dissecting channel.[2] Only a few cases of spontaneous healing of aortic dissection have been reported.[2,5] A retrospective study revealed only four cases.[5] A longitudinal study over 27 years identified five cases on autopsy.[2]

Transesophageal echocardiography is the best imaging modality for the diagnosis of acute aortic dissection.[6] It has high sensitivity (97-99%) and specificity (reaching 100% by the addition of M mode)[6,7], and is considered a class I indication.[8] It is particularly important for the proximal ascending aorta and aortic valve. The CT scan has a good sensitivity (83-98%) and specificity (87-100%).[6] However, the sensitivity to detect intimal flap is low (less than 75%).[9] It is a class II indication[8] and is superior for the imaging of the aortic arch vessels.[10] MRI is comparable to the TEE in sensitivity and specificity, but usually is not performed in the acute settings.[11] It is the modality of choice for chronic dissection.[8]

Our case had many interesting features. First, the patient presented with ischemic stroke instead of typical chest pain and was completely free of chest pain during his hospitalization. The aortic dissection apparently was healed and sealed spontaneously at the time of diagnosis which is a rare outcome. In addition, the neurologic symptoms and signs resolved completely in a few months. The combination of these rare events in the same patient made this case unusual. To our knowledge, no similar cases have been reported in the literature.

Aortic dissection should be suspected in young patients with ischemic stroke, especially in the absence medical risk factors. This case also emphasized the importance of TEE as a diagnostic tool for the diagnosis of acute aortic dissection and as a workup for the patient with ischemic stroke. TEE should be interpreted carefully as a subtle abnormality, such as the intimal flap, may be missed easily.

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Keywords: aortic dissection, stroke, ischemia, case report

Should Vitamin D Screening be a Part of Primary Care?

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Introduction

Vitamin D is a steroid hormone that regulates transcription of over 900 genes and is involved in nearly every organ system in the human body.[1] Vitamin D insufficiency and deficiency are increasing in prevalence worldwide, yet are commonly unrecognized clinically, even though serum vitamin D levels can be measured, and vitamin D repletion is inexpensive and well tolerated.

Classic manifestations of vitamin D deficiency include symmetric low back pain, proximal muscle weakness, myalgias, and bone pain.[1] Most cases of deficiency or insufficiency in the modern era, however, are not accompanied by such dramatic symptoms. Nonetheless, vitamin D screening has become a routine part of the primary medical care of patients in many medical practices. In spite of the broad practice of screening for vitamin D deficiency or insufficiency, we are left with conflicting data on what constitutes a normal vitamin D level, and even more controversy surrounding whether vitamin D should be screened routinely.

What is a normal vitamin D level?

Vitamin D status is assessed by measuring the prohormone 25-hydroxyvitamin D, which is an indicator of supply rather than function, as it must be hydroxylated in the kidney to form the active metabolite 1,25-dihydroxy-vitamin D. 25-hydroxyvitamin D is the most stable and plentiful metabolite of vitamin D in human serum, though, with a half-life of about three weeks, making it a very attractive metabolite for screening purposes.

Precisely defining vitamin D deficiency or insufficiency on the basis of 25-hydroxy-vitamin D values is a matter of much debate, as a normal range cannot be defined based on population norms, as might be the case with other hormone levels. A *functional* definition of optimal vitamin D status is the 25-hydroxyvitamin D level that maximally suppresses parathyroid hormone (PTH) secretion, as the major stimulus for PTH secretion is a low level of serum ionized calcium.[2] An alternative, albeit less elegant, definition might be the level at which there appears to be protection against adverse skeletal outcomes such as fracture and falls,[3] indices of bone remodeling, decreased bone mineral density in cross-sectional studies, or fractures in observational studies.[4,5]

In the cross-sectional National Health and Nutrition Examination Survey (NHANES III) survey, serum 25-hydroxyvitamin D concentration was associated with bone mineral density in community-dwelling women and men aged at least 20 years and up.[6] A cause-and-effect relationship, however, was difficult to prove, given that low vitamin D intake and low bone density might simply reflect that healthier persons who exercise more (thus have greater bone density) may spend more time outside in the sun (thus have higher 25-hydroxyvitamin D levels).[7,8]

The Women's Health Initiative calcium and vitamin D supplementation trial revealed that hipbone mineral density was 1.06 percent higher in women receiving calcium and vitamin D than in women

receiving placebo after nine years, but the lumbar spine total bone mineral density in supplemented subjects did not differ significantly from those receiving placebo during this interval.[8,9] In the nested case-control study, the 25-hydroxyvitamin D baseline level was 46.0 +/- 22.6 nmol/L among participants who had hip fracture and 48.4 +/- 23.5 nmol/L among controls (p = 0.17). No statistically significant interactions were found between calcium with vitamin D supplementation and baseline 25-hydroxyvitamin D level with respect to either hip or total fractures.[8]

A cross-sectional, observational study conducted at 61 sites across North America showed that 52 percent of postmenopausal women receiving therapy for osteoporosis had 25-hydroxyvitamin D levels of less than 30 ng/ml.[4] As it stands, most experts define vitamin D deficiency as a serum 25-hydroxyvitamin D level of less than 20 ng/mL (50 nmol/L) and insufficiency as a serum 25-hydroxyvitamin D level of 20 to 30 ng/mL (50 to 75 nmol/L).[5,10]

Two rationales exist for setting the low end of the normal range for 25-hydroxyvitamin D at 30 ng/ml.[11] First, the serum level of parathyroid hormone (PTH) rises when the vitamin D level falls below 30 ng/ml. Second, active calcium absorption is optimal when the vitamin D level is 30 ng/ml.[12,13] However, an Institute of Medicine[14] report questions both of these tenets.[15]

More recently, vitamin D insufficiency has been used to describe low levels of serum 25-hydroxyvitamin D that may be associated with other (non-skeletal) disease outcomes.[9] Interpreting the import of a serum level of 25-hydroxyvitamin D in the insufficient range (i.e., 10-30 ng/ml) is challenging for at least three reasons. First, most reference laboratories have raised the lower boundary of normal range to 30 ng/ml.

Second, the precision and accuracy of various vitamin D assays, especially in non-reference laboratories, remains problematic. High performance liquid chromatography is considered the gold standard method, but liquid chromatography-tandem mass spectrometry is currently among the most accurate measures of the separate contributions of both 25-hydroxyvitamin D2 and D3 to total 25-hydroxyvitamin D concentrations.[4] Different 25-hydroxy-vitamin D assays, though, yield markedly differing results; so different that whether an individual is found to have low or normal vitamin D status sometimes may be a function of the laboratory used. The chemiluminescent assay tends to give higher values of 25-hydroxyvitamin D. In a study in which a single serum sample showing adequate vitamin D status was sent to multiple laboratories, the level was correctly identified as adequate in one laboratory, but was considered insufficient in others, with differences of up to 17 ng/ml.[16] This discrepancy between labs and between assays has led to calls for measurement of 25-hydroxyvitamin D to be standardized.

Third, seasonal variation exists in both exposure to sunlight and in dietary intake of vitamin D, with levels typically highest during summer and lowest during winter.[5,17] A study of Asian adults in the United Kingdom showed that 82 percent had 25-hydroxyvitamin D levels less than 12 ng/ml during the summer season, with the proportion increasing to 94 percent during the winter months.[18] Vitamin D stored in body fat is released during winter, when vitamin D cannot be produced.

Previously, according to the World Health Organization (WHO), a 25-hydroxyvitamin D level below 10 ng/ml was classified as deficient and a level below 20 ng/ml was classified as insufficient.[13] However, with relatively recent changes in laboratory reference ranges, a normal level

now is defined by WHO as 30-76 ng/ml (75-190 nmol/L).[4,13,19]

The 2011 Dietary Reference Intake (DRI) for vitamin D based on bone health outcomes suggested that levels of 16 ng/ml meet the needs of approximately half the population and levels of at least 20 ng/ml meet the needs of 97.5% of the population (similar to the Required Dietary Allowance; RDA).[14] In 2010, the International Osteoporosis Foundation issued a statement on vitamin D status, based on observational data, recommending a target serum vitamin D level of 30 ng/ml in all elderly persons and vitamin D intakes as much as 2000 IU/day.[13]

Should we screen patients for vitamin D deficiency?

Given the conflicting but generally positive data outlined above, two arguments can be made in regards to vitamin D screening and/or treatment.

Patients routinely should be screened for vitamin D deficiency.

Patients should be screened for vitamin D deficiency for two reasons. First, screening detects potential vitamin D-associated disease states. Second, screening better determines the amount and duration of vitamin D supplementation needed to treat the disease state in question.

The serum 25-hydroxyvitamin D level is the best indicator for judging vitamin D status in patients with potential vitamin D-related disease states.[20] For example, severe deficiency (< 10 ng/mL) could be associated with osteomalacia or rickets, and moderate deficiency (10-25 ng/mL) may be associated with an increased risk of osteoporosis or secondary hyperpara-thyroidism.

Establishing the patient's untreated vitamin D level will give insight into the type of bone disease present, if any, and reduce the likelihood of causing harm through over-supplementation. Vitamin D toxicity causes hypercalcemia typically at serum levels over 120 ng/ml, and most often when it is consistently greater than 150-200ng/ml, although toxicity has been reported in patients with normal renal function and without primary hyper-parathyroidism at levels as low as 80 ng/mL.[9,13,21,22] The effects of toxicity (hypercalciuria, nephrocalcinosis, and calcium containing kidney stones) may take up to 6-9 months to abate after stopping vitamin D supplementation.

It commonly is assumed that the serum 25-hydroxyvitamin D level will increase by 1 nmol/L for every 57-100 IU of daily vitamin D intake taken as a loading dose, but this does not necessarily account for body weight and vitamin D metabolism.[13,23] Knowing the 25-hydroxyvitamin D level at baseline allows for a calculation of the amount of vitamin D supplementation needed to achieve a target vitamin D level, accounting for body weight:

Δ 25-hydroxyvitamin D = 0.025 x (dose IU/kg body weight)

therefore,

Loading Dose = 100 x (Desired Actual ng/mL of 25-hydroxyvitamin D) x Weight (kg)

This formula is not valid for cases of malabsorption, and its accuracy is unknown for patients over 125 kg. It also does not calculate the required maintenance dose.[23]

In addition to supplying information needed to calculate the required dose of vitamin D, knowledge of a baseline vitamin D level theoretically can help with timing of therapies. For example, administration of anti-resorptive therapy (e.g., bisphos-phonates, estrogen, raloxifene, or denosumab) to a vitamin D deficient patient

with osteomalacia may cause severe hypocalcemia.[24] Such a patient would need to normalize her vitamin D level before starting antiresorptive therapy.

Patients with suspected vitamin D deficiency should be treated empirically.

The serum 25-hydroxyitamin D level is an expensive test, and the cost is compounded when one considers that many patients deemed insufficient will undergo testing two or more times. No evidence-based consensus guidelines exist regarding screening for vitamin D deficiency/ insufficiency or for using serum markers for medical management of individual patients.[15] A more reasonable interpretation of current literature suggests that physicians should judge, based on an individual patient's risk of insufficiency or deficiency of vitamin D, whether measuring the 25-hydroxyvitamin D level will assist in diagnosing disease and/or significantly change medical management.

The National Health and Nutrition Examination Survey III data revealed that more than 90 percent of the pigmented population of the United States (Blacks, Hispanics, and Asians) now suffer from vitamin D insufficiency (defined as a 25-hydroxyvitamin D level less than 30 ng/ml), with nearly three-fourths of the white population in the United States also being vitamin D insufficient.[19,25] In general, males, children, leaner persons, and non-Hispanic whites have higher 25-hydroxyvitamin D concentrations than do females, adults, obese persons, non-Hispanic blacks, and Mexican-Americans.[26]

Conditions that cause very low levels (i.e., < 10 ng/ml) of 25-hydroxyvitamin D include use of anticonvulsant medications (e.g., phenobarbital, phenytoin) and long-term use of glucocorticoids, rifampin, cholestyramine,[5,27,28] poor dietary intake plus negligible sun exposure, or mal-absorption due to inflammatory bowel disease, gluten sensitive enteropathy, gastric surgery, biliary disease, or intestinal overgrowth.[10,13] These observations indicate that a person's risk for vitamin D deficiency could be established in many cases without an expensive laboratory study, and that the resulting financial resources could alternatively be put toward vitamin D replacement.

The very values defining vitamin D insufficiency are a moving target. 25-hydroxyvitamin D levels tend to be seasonal in the Midwest. Should a value of 30 ng/ml be sought all twelve months of the year, or should a winter level of 20 ng/ml be considered the "seasonal equivalent" of a summer value of 30 ng/ml? The long-term data do not exist to make such a distinction.

When laboratories across the US began using 30 ng/ml as their cut-off between sufficient and insufficient vitamin D blood levels, many physicians began instituting vitamin D supplementation in their patients. Since the Institute of Medicine's (IOM) decision to recognize a level of 20 ng/ml as meeting the requirements of 97.5% of the population, many of those same patients would now be considered replete without supplementation.[14]

Empiric supplementation of vitamin D appears safe, and the IOM raised its daily recommendations, stating most Americans and Canadians up to age 70 need no more than 600 IU/d and that older patients may need as much as 800 IU/d, along with diet and sunlight, to maintain health.[14] To illustrate the apparently wide therapeutic window of vitamin D though, the same report increased the upper limit of safe supplementation to 4,000 IU (100 mcg/day) for adults. Typical sun exposure of a person in a bathing suit of one minimal erythematic dose (which causes a slight pinkness to the skin) is equivalent to ingesting 20,000 IU of vitamin D.[29]

Summary

Low vitamin D status is increasing in prevalence worldwide. The role of screening for vitamin D deficiency in routine medical care though is still uncertain. Unresolved issues of vitamin D testing include definition of a normal serum level; prediction of a new serum vitamin D level as a function of dosage of vitamin D, given complex patient factors including age, endogenous production, season and geographic locale, ethnic background, diet, and underlying health conditions; and the fact that epidemiological studies appear to show different effective vitamin D levels for different disease states.

Large-scale randomized clinical trials and consensus cut-points for vitamin D level are needed to avoid both under- and over-treatment. Studies should be conducted with the goals of: 1) demonstrating a response to vitamin D supplementation as a function of vitamin D concentration with consideration of other patient variables, and 2) coming to agreement upon a 25-hydroxyvitamin D serum concentration goal to be aimed for through vitamin D supplementation for specific disease states.

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Key words: vitamin D, screening, diagnosis, primary health care

The Electrocardiogram and Drug-Induced Arrhythmias

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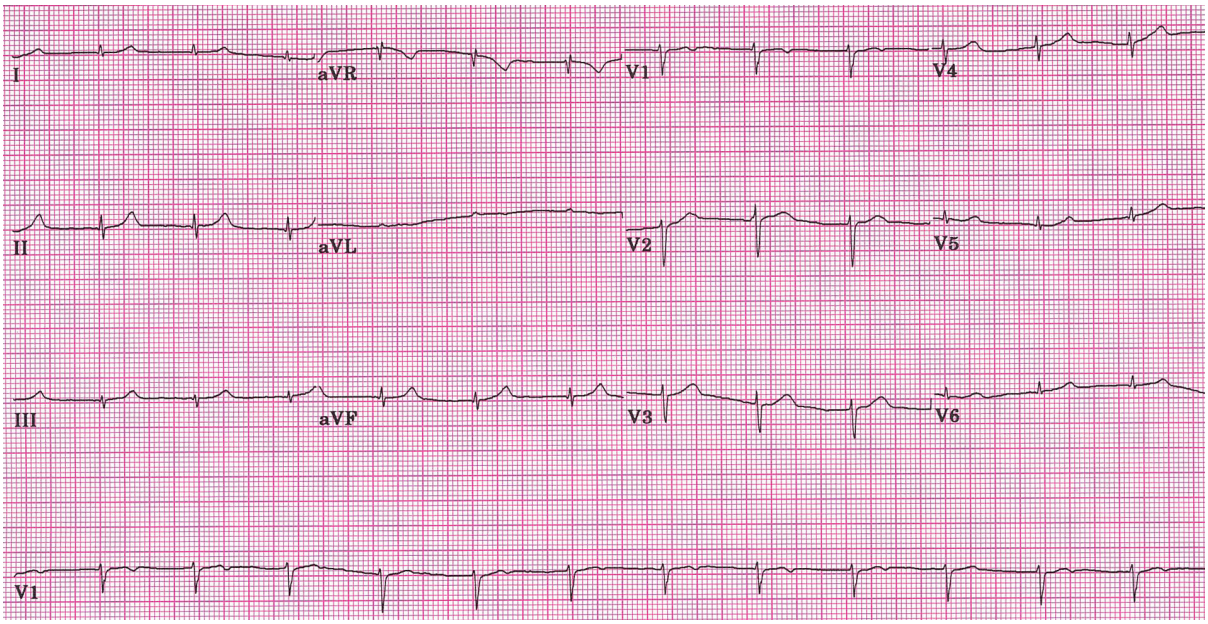
A 72-year-old male with a previous medical history consistent with chronic systolic heart failure presented for frequent episodes of generalized fatigue and shortness of air for the past week. The patient noted that his symptoms started a few days after he began a new anti-fungal medication. The initial echocardiogram is shown below.



What is the most likely diagnosis?

A) Long QT syndrome
B) Digoxin toxicity
C) Sick sinus syndrome
D) Hypocalcemia

CORRECT ANSWER: B

The ECG revealed a narrow QRS complex rhythm at a rate of 78 beats/minute without clearly visualized P waves, consistent with accelerated junctional rhythm. In the setting of chronic heart failure, this is often caused by digitalis toxicity. Low voltage is evident in the limb leads (QRS amplitude < 5 mm) which may be due to pleural effusion, pericardial effusion, or restrictive, infiltrative, or severe ischemic cardiomyopathy. Further questioning revealed this patient was on digoxin therapy and recently started anti-fungal therapy. His diuretic regimen increased which most likely led to his digoxin toxicity.

Discussion

Digoxin is a complex agent in that its mode of action, inhibition of sodium-potassium adenosine triphosphatase, affects multiple cellular processes, including several critical to cardiac myocyte function.[1] Digoxin also is extremely toxic, not surprising in view of its apparent role in nature as a toxin evolved by plants to kill mammals. Digoxin has a low therapeutic index and it should be monitored carefully by serum blood levels. The various clinical conditions and drug interactions that can alter digoxin's pharmacokinetics also are reflected in the serum digoxin level. The optimal trough digoxin serum level is 0.5 to 1.0 ng/mL. In patients with heart failure, overt clinical toxicity tends to emerge at serum concentrations greater than 2.0 ng/mL, but substantial overlap in serum levels exists among patients exhibiting symptoms and signs of toxicity and those with no clinical evidence of intoxication.

Disturbances in cardiac impulse formation, conduction, or both are the hallmarks of digitalis toxicity.[2] Among the common electrocardiographic manifestations are ectopic beats of AV junctional or ventricular origin, first-degree AV block, an excessively slow ventricular rate response to atrial fibrillation, or an accelerated AV junctional pacemaker. These manifestations may require only dosage adjustment and monitoring. Sinus bradycardia, sinoatrial arrest or exit block, and second- or third-degree AV conduction delay often respond to atropine, but temporary ventricular pacing sometimes is necessary and should be available. Neurological or gastrointestinal complaints also can be manifestations of digitalis toxicity. Occasionally, gynecomastia results from digoxin administration, due to similarity with estrogen's structure.

Oral potassium administration often is useful for management of atrial, AV junctional, or ventricular ectopic rhythms, even when the serum potassium is in the normal range, unless high-grade AV block also is present.[1,2] However, potassium must be monitored carefully to avoid hyperkalemia, especially in patients with renal failure. Magnesium may be useful in patients with atrial fibrillation in an accessory pathway in whom digoxin administration has facilitated a rapid accessory pathway-mediated ventricular response.[1] Again, careful monitoring is required to avoid hypermagnesemia.

Potentially life-threatening digoxin or digitoxin toxicity can be reversed by antidigoxin immunotherapy.[1] Purified Fab fragments from digoxin-specific antisera are available at most poison control centers and larger hospitals in North America and Europe. Clinical experience in adults and children has established the effectiveness and safety of antidigoxin Fab in treating life-threatening digoxin toxicity, including cases of massive ingestion with suicidal intent.

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