Remote diagnosis of cervical neoplasia: 2 types of telecolposcopy compared with cervicography

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Practice recommendations

- Computer-based telecolposcopy and network telecolposcopy detected more cervical neoplasia than cervicography.
- Computer-based telecolposcopy could provide many women with greater access to expert diagnostic services.

Telemedicine enables doctors in rural areas or areas with poor medical service to consult with experts at distant locations. Telecolposcopy and cervicography both enable remote diagnoses of the cervix. The 2 methods differ in equipment, operations, image format, timeliness of consultation, and probably cost. However, these diagnostic approaches have not been compared previously. The purpose of this study was to compare the accuracy of telecolposcopy and cervicography with on-site colposcopy in the remote evaluation of women with potential cervical neoplasia.

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TELECOLPOSCOPY AND CERVICOGRAPHY

Telecolposcopy involves a distant expert colposcopist's evaluation of women with potential lower genital tract neoplasia.[1] Existing telemedicine network and computer systems provide an audiovisual interface between local colposcopists and expert colposcopists at other locations.[2] For health systems already using computer or video networks, telecolposcopic consultation can be implemented with only small additional charges per examination.[2] Telecolposcopy services may improve health care access for women in medically underserved areas.[1]

Cervicography is distant evaluation of 2 photographs taken of the cervix following 5% acetic acid application.[3] A special 35-mm camera is used to take these images. The end product, developed at a central processing center, resembles a low-magnification colposcopic photograph. Certified evaluators interpret these images, classifying them as negative, atypical, or positive.

Cervicography is used primarily as an adjunct test to the Papanicolaou (Pap) smear.[4] It has also been evaluated as an intermediate triage test for evaluating women with mildly abnormal Pap smear results.[5–8]

METHODS

Women aged 18 years or older who came to 1 of 2 rural clinic sites for a colposcopic examination were enrolled in the trial after signing an institutional review board–approved informed consent document. We included women with a recent abnormal Pap smear report or a lower genital tract finding that required further evaluation by colposcopy. The exclusion criteria were pregnancy, severe cervicitis, heavy menses, refusal to participate, or technical problems with the telecolposcopy or cervicography equipment.

Both clinics were part of the Medical College of Georgia Telemedicine Network. This system uses sophisticated telecommunications equipment to provide distant consultation services to clinicians practicing in rural areas of the state.[1] Small change-coupled device cameras were attached to the colposcopes at the 2 clinics.

For network telecolposcopy, images were transmitted using the network's existing hardware and high-speed telecommunication lines. For computer telecolposcopy, personal computers (DIMS, DenVu, Tucson, Ariz) were also used to capture and transmit images to a computer at the Telemedicine Center. These digitized images were transmitted by modem via telephone lines.[2] Cerviscopes (35-mm cameras) supplied by the manufacturer (NTL Worldwide, Fenton, Mo) were used to acquire cervigrams (photographs).

Pertinent clinicians received appropriate training to take cervigrams. Certified evaluators interpreted the images according to company protocol and returned a standardized report to the investigators at a later date.

Study design

The study design has been described in detail previously.[1,2] Briefly, subjects were initially examined by 1 of 3 on-site, university-based expert colposcopists, who took 2 cervigrams of each patient, and then conducted a colposcopic examination independently.

For health systems with computer or video networks, telecolposcopy can be implemented at minimal cost

A local clinician then completed another colposcopic examination, including histologic sampling, if indicated. This examination was observed simultaneously by another expert at a telemedicine center. Prior to obtaining histologic samples or using dilute Lugol's iodine solution, the local clinician captured 2 cervical images (low and high magnification) using the computer telemedicine system. These images were then transmitted to the expert at the telemedicine center for independent interpretation.

A third expert colposcopist interpreted the video and computer images at a later time. However, these third interpretations were not considered in this report. Colposcopists were blinded to each other's clinical diagnoses. However, all colposcopists were informed of the subject's referral cervical cytology results and other pertinent history.

Data analysis

Each subject had 2 observations using each of the 3 colposcopy methods (on-site, network, and computer-based), and a single observation using cervicography. On-site colposcopy, consisting of the observations of the on-site expert and local colposcopist, was considered for reference purposes. Agreement with histologic results was calculated for each method, across all histologic diagnoses together and separately by diagnosis.

Sensitivity and specificity estimates were calculated using 2 definitions of disease: (1) normal versus any other histologic diagnosis, and (2) normal or cervical intraepithelial neoplasia 1 (CIN 1) versus any more severe diagnosis. The primary analysis model was complete block analysis of

There was no significant difference between colposcopy, telecolposcopy, and cervicography in detecting CIN 1

variance, with subjects included as blocks in the analysis to account for the multiple observations on the same subjects. Nonparametric comparisons of proportions of agreement with histology, sensitivity, and specificity among the methods were made using permutation tests. Post-hoc comparisons were made using a Tukey test; 95% confidence intervals (CIs) were calculated for all point estimates. Adjustment for dependence among multiple observations per subject was made by basing these tests and CIs on least-squares means.

The available sample sizes for all analyses were adequate to ensure approximate normality of the estimated means. Power to detect, at α=.05, a difference in agreement of 15% between cervigram and the other evaluation methods, was estimated using Monte Carlo simulations. Data were simulated using the observed levels of agreement for on-site, network, and computer telecolposcopy, and specifying a difference of 15% between cervicography agreement and the maximum of the other methods' agreement. Power estimates were based on analysis of 1000 simulations. SAS release 8.02 was used for all calculations (SAS, Inc, Cary, NC).

RESULTS

A total of 264 subjects were enrolled in the trial, but the total number of subjects considered differed depending on the various analyses of interest. The demographic data of this study cohort have been published previously.[1]

Briefly, the subjects' mean age was 31.7 years and mean parity was 2.1. Subjects presented with a wide range of prior cervical cytology results: 20.4% normal, 29.2% atypical squamous cells of undetermined significance, 40.4% low-grade squamous intraepithelial lesion, 7.3% high-grade squamous intraepithelial lesion, and 2.7% atypical glandular cells of undetermined significance. Histology results included all levels of CIN (52.9% CIN 1 and 13.4% CIN 2 or 3), and endocervical histologic sampling results were reported as both positive and negative for neoplasia.

The agreement between telecolposcopic/cervicography impressions and histology were estimated (**Table 1**). Data for on-site colposcopy was also considered for reference purposes.

When all histologic diagnoses were considered, there was no statistically significant difference in the rates of agreement for colposcopy, the 2 types of telecolposcopy, and cervicography. This was also true if only cases of CIN 1 were examined.

However, a statistically significant difference was noted between agreement rates for computer-based telecolposcopy (63.95%) and on-site colposcopy (47.7%, *P*=.03, Tukey test) for normal histology. A statistically significant difference was also found between agreement rates for on-site colposcopy (50.0%) and cervicography (19.1%, *P*=.04, Tukey test) for women with biopsy-proven CIN 2 or 3. If all histologic diagnoses were considered, the study provided 85% power to detect a difference in agreement of 15% among the evaluation methods.

We also estimated the sensitivity and specificity of the four diagnostic methods to detect cervical neoplasia (**Table 2**). A statistically significant difference was found in observed sensitivity between on-site colposcopy (47.7%) and cervicography (18.2%, *P*=.04, Tukey test) when a positive threshold of at least CIN 2 was considered. The difference was not significant, however, if the lower positive test threshold of at least CIN 1 was considered.

A statistically significant difference in specificity was noted between computer-based telecolposcopy (64.0%) and on-site colposcopy (47.7%, *P*=.03, Tukey test) at a positive threshold of at least CIN 1. The study provided a power of 71% and 60% to detect differences of 15% in sensitivity and specificity, respectively, using the CIN 1 threshold. Using CIN 2 as the positive threshold,

TABLE 1

Colposcopic, telecolposcopic, and cervicographic agreement with histology

Histology[a]	On-site colposcopy[b]	Network telecolposcopy[c]	Computer-based telecolposcopy[d]	Cervicography[e]	*P* [f]
All diagnoses					
%	56.9	53.5	55.5	52.4	
n/N[g]	165/290	155/290	161/290	76/145	.66
95% CI[h]	52.0–61.8	48.5–58.3	50.6–60.4	45.5–59.4	
Normal					
%	47.7	48.8	63.95	58.1	
n/N	41/86	42/86	55/86	25/43	.03[i]
95% CI	39.1–56.2	40.3–57.4	55.4–72.5	46.0–70.2	
CIN 1					
%	64.4	58.8	56.9	58.8	
n/N	103/160	94/160	91/160	47/80	.47
95% CI	57.7–71.1	52.0–65.5	50.2–63.6	49.3–68.2	
CIN 2/3					
%	50.0	45.2	35.7	19.1	
n/N	21/42	19/42	15/42	4/21	.04[j]
95% CI	36.6–63.4	31.9–58.6	22.3–49.1	0.1–38.0	

a. Cervical biopsy result.
b. Colposcopy conducted at rural site by site expert and local colposcopist.
c. Colposcopy observed by 2 distant experts at telemedicine center using telemedicine network equipment.
d. Colposcopy observed by 2 distant experts at telemedicine center using computer-based system.
e. Cervicography interpreted by a single cervical evaluator.
f. *P* value from permutation test.
g. The numerator is the number of observations in agreement with histology; the denominator is the number of observations with 2 per subject for on-site, network, and computer-based, 1 observation per subject for cervicography.
h. 95% confidence intervals based on normal approximation, adjusted for repeated measures.
i. Computer-based > on-site, Tukey's test.
j. On-site > cervicography, Tukey's test.

CI, confidence interval; CIN, cervical intraepithelial neoplasia

TABLE 2

Sensitivity and specificity of tests to detect cervical neoplasia

Positive threshold[a]	Assessment device	Sensitivity	Specificity	LR+[b]	LR-[c]
CIN 1	On-site colposcopy[d]			1.2	0.8
	% (95% CI)[f]	60.8 (54.8–66.7)	47.7 (39.1–56.2)		
	n/N[e]	124/204	41/86		
	Network telecolposcopy[g]			1.1	0.9
	% (95% CI)	55.4 (49.6–61.2)	48.8 (40.3–57.4)		
	n/N	113/204	42/86		
	Computer-based telecolposcopy[h]			1.4	0.8
	% (95% CI)	52.0 (46.0–57.9)	64.0(55.4–72.5)		
	n/N	106/204	55/86		
	Cervicography[i]			1.2	0.9
	% (95% CI)	50.0 (41.6–58.4)	58.1 (46.0–70.2)		
	n/N	51/102	25/43		
P[j]		.1	.3[k]		
CIN 2	On-site colposcopy			1.2	0.9
	% (95% CI)	47.7 (34.9–60.5)	58.5 (53.2–63.8)		
	n/N	21/44	144/246		
	Network telecolposcopy			1.0	1.0
	% (95% CI)	43.2 (30.4–56.0)	55.3 (50.0–60.6)		
	n/N	19/44	136/246		
	Computer-based telecolposcopy			0.8	1.1
	% (95% CI)	34.1 (21.3–46.9)	59.4 (54.0–64.7)		
	n/N	15/44	146/246		
	Cervicography			0.4	1.4
	% (95% CI)	18.2 (0.1–36.3)	58.5 (51.0–66.0)		
	n/N	4/22	72/123		
P		.049[l]	.74		

a. Threshold considered positive (ie, disease vs nondisease).
b. Likelihood ratio of positive test = sensitivity / (1 - specificity).
c. Likelihood ratio of negative test = (1 - sensitivity) / specificity.
d. Colposcopy conducted at rural site by site expert and local colposcopist.
e. The numerator is the number of observations that led to correct diagnosis; the denominator is the number of observations with 2 per subject for on-site, network, and computer-based, 1 observation per subject for cervicography.
f. 95% confidence intervals based on normal approximation, adjusted for repeated measures.
g. Colposcopy observed by 2 distant experts at telemedicine center using existing telemedicine network equipment.
h. Colposcopy observed by 2 distant experts at telemedicine center using computer-based system.
i. Cervicography interpreted by a single certified evaluator.
j. P from permutation test.
k. Computer-based > on-site, Tukey test.
l. On-site > cervicography Tukey test.

CI, confidence interval; LR+, positive likelihood ratio; LR-, negative likelihood ratio; CIN, cervical intraepithelial neoplasia.

the power to detect this 15% difference was 24% and 81% for sensitivity and specificity, respectively.

With a laptop and cell phone, health care providers worldwide could have access to expert evaluation services

DISCUSSION

Until recently, cervicography had been the only type of remote diagnostic system available for the evaluation of women with potential lower genital tract neoplasia. With the advent of telemedicine during the past decade, expert-level health care has now become more readily available to patients previously isolated from this important resource.

The future of telecolposcopy

Because of its nature, telecolposcopy may also be well suited to assist in the evaluation and management of women with lower genital tract neoplasia. Computer-based telecolposcopy has the potential to support clinical sites located wherever standard telephone service exists. Cellular telephone systems now broaden access to near-global availability. Soon, assuming sufficient funding is obtained, the provision of expert-enhanced colposcopy may become a reality for all women. However, universal availability may be irrelevant if computer-based telecolposcopy performs at a substandard level.

Telecolposcopy vs cervicography

We have demonstrated that telecolposcopy was at least as effective as cervicography for detecting cervical cancer precursors. Although the difference was not statistically significant, both network and computer-based telecolposcopy systems detected a higher percentage of women with CIN 2 or 3 than cervicography.

Our results also included on-site colposcopy. As anticipated, on-site colposcopy had the greatest sensitivity for disease detection at either positive test thresholds (at least CIN 1 and CIN 2). Ability to manipulate the cervix, stereoscopic viewing, longitudinal observation after 5% acetic acid application, and better resolution of the cervical epithelium and vascularity all favor on-site colposcopic diagnoses. Of the 2 telecolposcopy systems, network telecolposcopy had a slightly, but not significantly, greater sensitivity for detecting cervical cancer precursors compared with computer-based telecolposcopy.

Expert colposcopists' accuracy with interpretation of network (real-time) cervical images was similar to that for on-site colposcopy, as might be expected. Network telecolposcopy might be equated with remote video colposcopy. Previously we have shown that traditional optical colposcopy is equivalent to video colposcopy with respect to colposcopic/histologic agreement.[9]

Comparison of telecolposcopy systems

The computer-based telecolposcopy system used in our study was, in all fairness, more similar to cervicography. Each method involves evaluation of 2 static images. Computer-based telecolposcopy provides 2 digitized images, but of a low- and high-power magnification view of the cervix. In comparison, cervicography produces dual low-power magnification celluloid images (2 x 2 slides) of the cervix. The provision of a high-power cervical image may explain the better sensitivity of computer-based telecolposcopy. This one feature may be more valuable than the better image resolution obtained from cervicography. However, computer-based resolution appears to be sufficient to render diagnoses at a level equivalent to or better than cervicography.

These 2 "static" systems differ in other aspects as well. First, computer-based systems are nonproprietary. Several systems are commercially available and other colposcopists have devised their own unique systems using modifications of off-the-shelf technology. Although not available at the initiation of our trial, computer-based systems now have the capability of captur-

ing short video streams. These video segments should help improve the diagnostic ability of consulting colposcopists as demonstrated by our study.

Second, computer-based telecolposcopy can provide instantaneous consultation as opposed to cervicography, which generally takes a minimum of several weeks to receive a report. Computer-based telecolposcopy also allows interaction between the on-site provider and remote expert.

Third, cervicography is a screening test adjunct. The computer-based system was used as a colposcopy diagnostic adjunct. However, colposcopy could easily be adapted to provide the function of cervicography. A simple handheld miniature change-coupled device camera and light source could potentially replace a more expensive colposcope and video camera, or video colposcope. With an average laptop computer (with appropriate software) and cellular phone, health care providers of potentially all women in the world could have access to expert-level cervical evaluation services.

Finally, computer-based telecolposcopy images and associated data automatically become part of a modern electronic medical record. This format is more conducive to the direction toward which contemporary medicine is rapidly shifting. Consequently, computer-based telecolposcopy may offer clinicians superior, modern diagnostic services not previously available to women.

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