Yale School of Medicine

Evaluation of Anal Cancer Screening in 18–34-Year-Old Men Who Have Sex With Men Living With HIV

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Serina S Applebaum[1], Elizabeth Chan[1,2], Lydia Aoun-Barakat[1], Michael Virata[1], Ritche Hao[1], Amit C Achhra[1]

[1]Section of Infectious Diseases, Department of Medicine, Yale School of Medicine, New Haven, CT, USA, [2]Atrius Health, Medford, MA, USA

BACKGROUND

- Squamous cell carcinoma of the anus (SCCA) disproportionately affects men who have sex with men (MSM) living with HIV (LWH)
- Recent guidelines recommend annual anal cytology (anal papanicolaou smear [PAP]) for MSM LWH aged ≥35 years followed by high resolution anoscopy (HRA) for abnormal results to detect and treat high-grade squamous intraepithelial lesions (HSIL) before progression to cancer[1,2]
- There is a growing interest in whether SCCA screening age should be expanded to younger MSM, similar to the recommended cervical cancer screening age for women (21 years old)[3]
- Historically, our center had offered SCCA screening to younger MSM LWH
- **Purpose: to evaluate the prevalence and outcomes of anal cancer screening among MSM LWH under age 35** in order to clarify the appropriateness of an age-based screening threshold
  - To characterize the prevalence of cytologic and histologic abnormalities
  - To assess the PPV of cytology for histologic findings
  - To assess factors associated with abnormal screening results in this younger cohort
  - To describe characteristics of SCCA diagnoses in this age group in our cohort

METHODS

- Retrospective chart review of electronic health record (EHR) data from 2013-2023 of all anal cancer screening encounters (PAP or HRA) for MSM LWH seen in HIV clinic up to age 34 years at the time of testing
- We described summary statistics of anal PAP and HRA results, and positive predictive value of anal PAP (true positive count [HRA result] divided by test positive count [PAP result])
- We report HPV results, though it was not routinely tested in the past and only recently addedto clinical pathways
- We analyzed characteristics independently associated with abnormal PAP and HRA using mixed effects logistic regression, to account for multiple tests per person
- We described cases of incident SCCA diagnoses

RESULTS

Table 1. Descriptive characteristics of the study population

Characteristic	Overall, N = 216	PAP and/or HRA, N = 127	No PAP or HRA, N = 89	P-value
Age at first visit, years				0.86
18-24	70 (32%)	42 (33%)	28 (31%)	
25-29	80 (37%)	48 (38%)	32 (36%)	
30-34	66 (31%)	37 (29%)	29 (33%)	
Race/Ethnicity				0.66
Non-Hispanic White	51 (24%)	32 (25%)	19 (21%)	
Non-Hispanic Black	94 (44%)	51 (40%)	43 (48%)	
Hispanic	56 (26%)	34 (27%)	22 (25%)	
Other	15 (6.9%)	10 (7.9%)	5 (5.6%)	
Follow-up duration, years	3.1 (1.2, 5.2)	3.8 (1.8, 5.6)	1.6 (0.7, 4.2)	<0.001
Health insurance				0.46
Private	88 (41%)	56 (44%)	32 (36%)	
Public	104 (48%)	57 (45%)	47 (53%)	
None	24 (11%)	14 (11%)	10 (11%)	
Last CD4 T-cell count				0.39
>499	162 (75%)	100 (79%)	62 (70%)	
200-499	42 (20%)	21 (17%)	21 (24%)	
<200	11 (5%)	6 (5%)	5 (6%)	
Last viral load				0.27
Undetectable (<20)	142 (66%)	89 (70%)	53 (60%)	
Suppressed (20-1000)	48 (22%)	25 (20%)	23 (26%)	
Unsuppressed (>1000)	26 (12%)	13 (10%)	13 (15%)	
Had HPV vaccine	99 (46%)	58 (46%)	41 (46%)	0.95
Age at first vaccine	25 (21, 30)	26 (22, 30)	25 (20, 30)	0.83
Current or former smoker	103 (49%)	59 (46%)	44 (52%)	0.45

Table 2. Characteristics of anal PAPs, and HRAs following abnormal PAP

Characteristic	Anal cytology (n = 246)	HRA (n = 23)
Symptoms prompting testing	38 (15%)	11 (48%)
Age at test		
18-24	6 (10%)	5 (22%)
25-29	27 (45%)	8 (35%)
30-34	27 (45%)	10 (43%)
Years since HIV diagnosis	4.0 (1.0, 7.0)	3.5 (2.0, 7.0)
Cytology result		
Negative	124 (50%)	-
ASCUS	49 (20%)	-
LSIL	27 (11%)	-
HSIL	0 (0%)	-
Unsatisfactory	46 (19%)	-
HPV co-test result		
Positive	44 (19%)	-
Negative	28 (11%)	-
Indeterminate	19 (8%)	-
Not tested	155 (63%)	-
Biopsy result		
Negative	-	6 (26%)
LSIL (AIN 1)	-	6 (26%)
HSIL (AIN 2 or 3)	-	10 (43%)
SCC*	-	1 (4%)

* A second incident SCCA case is not reported in this table due to diagnosis by direct HRA with no preceding PAP

Table 3. Multivariable mixed effects logistic regressions for characteristics associated with ASCUS or worse cytology (N=246 PAPs) and for HSIL or worse histology (N=60 total HRAs)

	Cytology ASCUS or worse			Histology HSIL or worse		
Characteristic	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-value
Age at test (ref: 18-24)						
25-29	1.45	0.46 – 4.54	0.52	2.89	0.26 – 31.66	0.39
30-34	1.25	0.30 – 5.25	0.76	1.90	0.12 – 30.29	0.65
Race/ethnicity (ref: non-Hispanic White)						
Non-Hispanic Black	0.34	0.10 – 1.17	0.09	1.93	0.20 – 18.48	0.57
Hispanic	1.02	0.27 – 3.88	0.98	3.01	0.05 – 186.53	0.60
Other	0.77	0.12 – 4.99	0.78	0.00	0.00 – Inf	0.99
Health insurance (ref: Private)						
Public	0.44	0.15 – 1.29	0.14	3.20	0.61 – 16.80	0.17
None	1.98	0.46 – 8.48	0.36	1.74	0.02 – 154.37	0.81
Years since HIV diagnosis	0.92	0.80 – 1.06	0.24	1.09	0.83 – 1.43	0.54
Last CD4 T-cell count (ref: ≥500)						
<500	0.52	0.15 – 1.77	0.29	0.95	0.06 – 15.95	0.97
HIV viral load (ref: undetectable)						
Suppressed	2.72	0.77 – 9.65	0.12	2.98	0.38 – 23.47	0.30
Unsuppressed	2.27	0.45 – 11.46	0.32	0.92	0.01 – 71.26	0.97
Age at HPV vaccine (ref: never vaccinated)						
<26	0.89	0.25 – 3.11	0.85	0.20	0.01 – 2.74	0.23
≥26	0.33	0.10 – 1.10	0.07	3.22	0.20 – 51.52	0.41
Ever smoker	0.64	0.24 – 1.72	0.38	0.21	0.01 – 4.37	0.32
Symptoms prompting testing	8.08	2.27 – 28.83	**0.001**	1.47	0.17 – 12.54	0.72

*Models are adjusted for all variables listed in table, and for multiple observations on the same individual.

RESULTS

- 216 18-to-34-year-old MSM LWH were seen in HIV clinic, **127** of whom underwent anal cancer testing (PAP and/or HRA).
- About 46% had history of HPV vaccine.
- Of the 127 tested individuals, 58 (46%) had 2 or more PAPs, and 31 (34%) had 3 or more PAPs through age 34
- Of the total 246 total anal cytology tests performed, 76 (31%) were abnormal, 23 of which had a follow-up HRA (Table 2)
- The positive predictive value of any cytologic abnormality on PAP for HSIL on HRA biopsy was 47.8%. Cytology underestimated the severity of the lesion in many cases that had follow-up biopsy (zero HSIL diagnoses on cytology)
- 19% of all cytology results were unsatisfactory for evaluation
- Neither history of HPV vaccination nor age subgroup were associated with abnormal PAP or HRA biopsy (Table 3)
- Two individuals were diagnosed with SCCA, at ages 29 and 30. Both had CD4 T-cell nadir <20 cells/mm^3; neither had prior HPV vaccine; both diagnoses were local and established by HRA performed for resection of large symptomatic condyloma (not for screening; 1 never screened, 1 had asymptomatic screen 4 years prior)

CONCLUSIONS & DISCUSSION

- Over 10 years, uptake of anal cancer screening among young (18-34 years) MSM LWH was variable. Anal PAP had a high rate of ‘unsatisfactory’ samples and poor PPV for high-grade dysplasia
- Despite high prevalence of high-grade dysplasia in those undergoing HRA, SCCA diagnoses were rare overall (only 2 cases, both diagnosed early due to symptoms)
- Our findings are consistent with the only other major study in this age group in the literature.[4]
- Collectively, these findings support excluding younger (<35 years) MSM LWH from routine asymptomatic screening
- Our study was limited due to its retrospective nature, reliance on EHR data, small sample size, and low number of clinical outcomes

Discussion

- Any decision to change screening age carries clinical and resource implications. Our findings suggest excess routine screening of younger MSM LWH could lead to overdiagnosis, unnecessary procedures, and increased healthcare costs
- Increasing HPV vaccination in this high-risk population remains a public health imperative to prevent disease
- Expanding age cutoffs for SCCA screening should be empiric evaluation, ideally by an RCT powered for clinical outcomes

References: 1. National Institutes of Health, Centers for Disease Control and Prevention, HIV Medicine Association, and Infectious Diseases Society of America;2024.
2. Stier EA, Clarke MA, Deshmukh AA, et al. *Int J Cancer.* 2024;154(10):1694-1702. 3. Addison J, Guss C, et al. *Front Pediatr*. 2022;10:875184 4. Liu Y, Bhardwaj S, Sigel K, et al. *Int J Cancer.* 2024;154(1):21-27