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Research Article

Evolving Techniques for Cervical Cancer Screening and Diagnosis

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Abstract

Background: Metrorrhagia is defined as irregular uterine bleeding occurring between normal menstrual cycles. Unlike normal menstruation, metrorrhagia is irregular in frequency, duration, and volume. Understanding the etiology of metrorrhagia requires reviewing the hormonal regulation of the normal menstrual cycle.
Purpose: This abstract provides an overview of metrorrhagia, including epidemiology, etiology, diagnostic evaluation, management approaches, and future directions.
Main Body: Metrorrhagia has a variable prevalence depending on age and underlying causes. Etiologies include hormonal dysfunction leading to anovulatory cycles, uterine structural abnormalities like fibroids or polyps, systemic conditions affecting coagulation or thyroid function, and iatrogenic causes such as intrauterine devices. Diagnostic evaluation aims to elucidate the cause through history, physical exam, laboratory studies, and imaging like pelvic ultrasound or endometrial biopsy. Treatment targets the underlying etiology, using hormonal therapy to regulate ovulation or procedural interventions for structural abnormalities unresponsive to medical management. Traditional herbal medicines provide another historical approach to managing metrorrhagia, though most lack standardization. Looking forward, advances in genomics, biologics, and artificial intelligence may enable more personalized, targeted therapies.

Conclusion: metrorrhagia arises from diverse etiologies encompassing hormonal, structural, systemic, and iatrogenic causes. Diagnosis hinges on a thorough evaluation to direct appropriate treatment ranging from medications to surgery. Further research on individualized therapies promises progress in long-term management.

Key words: metrorrhagia; abnormal uterine bleeding; anovulation; endometrium; hormonal therapy; hysteroscopy; complementary medicine

1.Introduction

Oncogenic viruses such as human papillomavirus (HPV) and Epstein-Barr virus (EBV) play a pivotal role in the pathogenesis of cervical cancer. As depicted in **Figure 1**,

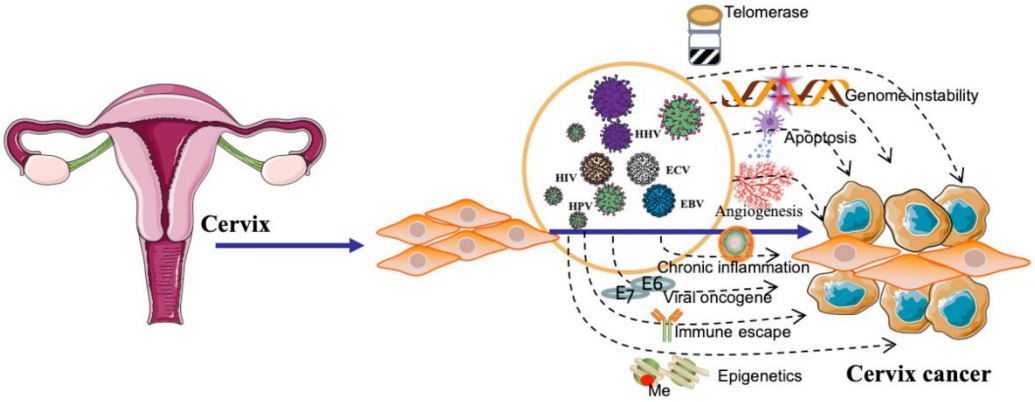

Figure 1. Cervical Cancer Pathogenesis Mediated by Oncogenic Viruses [1]

the expression of viral oncoproteins like HPV E6 and E7 results in the deregulation of cell cycle control and inhibition of tumor suppressors p53 and pRb. This leads to aberrant cell proliferation and accumulation of mutations. Additionally, viruses modulate the tumor microenvironment through immune evasion mechanisms, promotion of chronic inflammation, angiogenesis, and epigenetic changes that favor carcinogenesis. Viral infections can also activate telomerase to maintain telomere length and genome stability. Collectively, these viral-mediated effects override cell cycle checkpoints, enhance cell survival, and enable malignant transformation of cervical epithelial cells [1]. Cervical biopsy is a medical procedure in which a small amount of tissue is removed from the cervix for diagnostic examination [2]. It is typically performed when screening tests such as a Pap smear or HPV test indicate abnormal cellular changes in the cervix that could potentially represent precancerous lesions or cervical cancer [3]. Cervical biopsy is often recommended after an abnormal Pap smear result showing cellular irregularities. Pap smears check for changes in cells of the cervix that could indicate early or advanced cervical cancer. If abnormalities are detected, the next step is often colposcopy, which allows for a magnified view of the cervix. The colposcopy exam helps determine areas of concern that should be biopsied. Cervical biopsy may also be warranted with a positive HPV test, as certain high-risk HPV strains can cause cervical cancer. Persistent HPV infections, recurrent abnormal Pap results, or visible cervical lesions are other common reasons for performing cervical biopsy [4]. Cervical biopsy is typically performed by a gynecologist in an outpatient clinic setting. The patient is positioned as for a pelvic exam, and a speculum is used to visualize the cervix. The doctor applies a dilute acetic acid solution to highlight abnormal areas. Using forceps, a small sample of tissue is extracted from the suspicious region. Local anesthetic is generally administered prior to reduce discomfort. The removed tissue is preserved and sent to a pathology lab for analysis. Cell architecture and morphology are examined under a microscope to check for cancerous changes [5]. Patients may feel some menstrual-like cramping and pinching during the biopsy. Spotting or minor bleeding can occur after. Recovery is relatively quick, but patients are advised to avoid sexual intercourse, douching, and using tampons for 1-2 weeks post-biopsy to lower infection risk while the cervix heals. Over-the-counter pain medication can be used to manage discomfort. Potential complications like excessive bleeding, fever, or heavy discharge should prompt urgent follow-up with the physician [6]. If the biopsy detects precancerous cellular changes, close monitoring and treatment become crucial and early intervention improves outcomes. If results are negative, repeat screening at regular intervals is still needed. Patients should follow recommendations for additional testing and understand biopsy provides limited sampling. Close adherence to follow-up care is imperative. Cervical cancer screening techniques require periodic reevaluation as new technologies emerge. While cytology has served as the traditional screening mainstay, innovations like human papillomavirus (HPV) testing offer enhanced sensitivity [7]. However, the real-world performance of emerging screening modalities in clinical practice remains uncertain. This review comprehensively evaluates both established and novel approaches to cervical screening in order to provide updated evidence-based recommendations to practitioners on optimal integration of traditional and modern diagnostics.

II. Traditional Cervical Biopsy

The standard technique for cervical biopsy has remained relatively consistent in recent years. It is typically performed in the outpatient setting by a gynecologist. The patient is positioned on the exam table as for a pelvic exam, with feet in stirrups. The physician first inserts a speculum to visualize the cervix. After cleansing the cervix, a colposcope is used to magnify the view of the epithelial surface. A dilute acetic acid solution is applied, causing abnormal areas to appear white [8]. The physician uses forceps to grasp a small sample of tissue from the suspicious region of the cervix. A punch biopsy instrument may also be utilized to core out tissue. Local anesthetic is often injected at the site beforehand to minimize discomfort. The tissue is removed and sent to pathology for microscopic analysis. One or more samples may be taken depending on the appearance of the cervix. During the biopsy, patients usually tolerate the procedure well but may experience some cramping similar to menstrual pains and a pinching sensation on tissue removal. Mild spotting or bleeding can occur afterwards. Patients are advised to refrain from sexual intercourse, douching, and tampon use for 1-2 weeks following biopsy to lower risks of infection while the cervix heals. Over-the-counter analgesics can alleviate pain or cramps [9]. Potential complications include excessive bleeding, infection, or scar tissue on the cervix. Patients should watch for signs of fever, foul-smelling discharge, or heavy bleeding that requires prompt medical care. Routine follow-up is not needed after biopsy, but patients must comply with screening recommendations for repeat testing at regular intervals.

III. Alternative Innovations in Cervical Testing

In addition to the conventional Pap smear, several innovative cervical cancer screening approaches have emerged in recent years. These provide alternative options that are less invasive than traditional biopsy and aim to improve accuracy of detecting precancerous changes. One innovation is utilizing HPV DNA testing as the primary screening method, given that nearly all cervical cancers are caused by high-risk HPV strains. HPV testing has higher sensitivity for identifying women at risk compared to cytology alone. Self-collection of cervicovaginal samples at home for HPV testing also expands screening access [10]. Liquid-based cytology uses a sample suspension for Pap smears rather than directly smearing on a slide. This ThinPrep method decreases obscuring factors like blood and inflammation for more discernible cell analysis. However, its advantage over conventional Pap smears remains uncertain [11]. Some devices apply different spectroscopy techniques to cervical tissue. Raman spectroscopy uses laser light excitation to characterize biochemical changes. Electrical impedance spectroscopy measures electrical properties of the cervix to highlight abnormal changes. These methods attempt to provide objective, real-time

assessment [12]. While promising, most alternatives lack sufficient evidence and large-scale validation. HPV testing is furthest along for primary screening but still requires Pap co-testing currently. Self-sampling, liquid-based cytology, and spectroscopy techniques may improve screening accuracy but remain supplemental at this time. Their ultimate roles are still evolving.

III. 1. Advantages of Alternative Cervical Screening Methods

Alternative screening techniques offer several advantages compared to traditional methods like Pap smear and cervical biopsy. Most importantly, they are less invasive, eliminating the need for tissue removal. HPV testing and self-sampling only require a swab or lavage without specialist equipment. Spectroscopy is also non-invasive. This reduces discomfort and potential complications [13]. The alternatives can also enhance convenience and accessibility. At-home self-collection of samples empowers women to complete screening on their schedule. HPV testing may require less frequent intervals than annual Pap testing. Some spectroscopic devices enable real-time point-of-care assessment during a clinic visit [14]. Preliminary research indicates some alternatives can improve sensitivity and specificity for detecting cervical precancer and cancer. HPV testing appears to have higher sensitivity than Pap smear, making it less likely to miss abnormalities. Specificity may also increase by limiting false positives. Spectroscopy measures objective biomarkers rather than relying on cytology interpretation [15].

III. 2. Disadvantages and Limitations of Alternative Screening Methods

While innovative cervical screening techniques offer several advantages, important disadvantages and limitations remain. These newer approaches lack the abundant evidence and validation of conventional methods that have decades of extensive use. Large-scale clinical trials are still underway for technologies like HPV testing and spectroscopy. Real-world performance remains uncertain [16]. Implementing new screening systems also incurs significant upfront expenses for equipment, training, and quality assurance. These costs may not be sustainable in resource-limited settings. From a patient perspective, alternatives like spectroscopy are unlikely to be covered by insurance until efficacy is proven. Out-of-pocket costs may be prohibitive [17]. Most crucially, a key limitation is that abnormal alternative screening results still require follow-up with colposcopy and biopsy for confirmation. No alternative can definitively diagnose cervical precancer or cancer. Biopsy remains essential for obtaining pathology confirmation and guiding appropriate management. This two-step process reduces efficiency [18].

Feature	Traditional Cervical Biopsy	Alternative Screening Methods
Technique Used	Tissue removal with forceps or punch	HPV testing, liquid-based cytology, spectroscopy
Invasiveness	Invasive	Less or non-invasive
Evidence Level	Extensive validation over decades	Variable evidence, some still undergoing trials
Accuracy	Histology gold standard	Sensitivity may be higher or similar, specificity uncertain
Cost and Access	Procedure cost may limit access	Potentially lower cost, at-home sampling improves access

Table 3: comparing traditional cervical biopsy versus alternative screening methods:

IV. Traditional Medicine and Herbal Treatments

Complementary medicine approaches have historical roots in managing gynecological conditions [19]. Herbs like calendula, goldenseal, and myrrh have traditional uses related to cervical health, but current evidence on efficacy and safety remains limited [20]. Calendula (Calendula officinalis) flowers have anti-inflammatory properties that potentially treat cervicitis and cervical dysplasia. Traditionally prepared as tea or diluted tinctures, calendula may help relieve related pain and irritation. However, rigorous studies are lacking to support real-world benefits and optimal dosing [21]. Goldenseal (Hydrastis canadensis) contains the antimicrobial compound berberine. It has traditionally been used topically or orally for cervical inflammation and dysplasia due to its hypothesized antiseptic and tissue regenerating effects. But clinical evidence is inadequate to demonstrate efficacy, and goldenseal can cause adverse reactions like gastrointestinal upset [22]. Myrrh (Commiphora molmol) resin also has historical medicinal use for gynecological conditions. Myrrh's antimicrobial and astringent qualities may help alleviate cervicitis symptoms. But robust trials confirming therapeutic efficacy for precancerous cervical changes are unavailable currently [23]. While these herbs are relatively safe in typical doses, risks like allergic reactions exist. Patients should use caution and advise their healthcare provider regarding usage due to potential interactions with standard medical therapies. For example, goldenseal may impact efficacy of cytochrome P450 substrates like oral contraceptives [24]. Additionally, none of these herbal remedies have proven curative effects, and relying solely on unconfirmed traditional medicine while ignoring conventional screening and treatment for cervical dysplasia would be unwise.

Herb/Medicine	Traditional Uses	Current Evidence Limitations
Calendula	Anti-inflammatory, treat cervicitis and dysplasia	No rigorous efficacy studies
Goldenseal	Antimicrobial, anti-inflammatory	Inadequate clinical evidence, adverse effects possible
Myrrh	Antimicrobial, anti-inflammatory	No robust trials confirming efficacy

Table 2: herbal supplements and traditional medicine for cervical health:

V. Role of Nanomedicine

Nanotechnology is an emerging field showing promising applications in cervical cancer medicine [25]. At the nanoscale, materials exhibit unique properties that can be harnessed for improved therapies and diagnostics [26]. Nanoparticle-based drug delivery represents one major area of cervical cancer nanomedicine research. Nanoparticles like liposomes, dendrimers, carbon nanotubes, and polymeric formulations can encapsulate chemotherapeutic or other drug cargo. This enables targeted delivery to cervical tumor tissue. Benefits include prolonged drug circulation, controlled release kinetics, and enhanced specific uptake by cancer cells. This improves anti-tumor efficacy while reducing systemic toxicity [27]. In addition, nano-enabled diagnostic approaches like quantum dots, gold nanoparticles, and magnetic nanoparticles are being studied. These ultrasensitive and stable nanoprobes could enable earlier detection of precancerous cervical changes through enhanced imaging and biosensing capabilities [28]. However, nanomedicine faces substantial barriers to clinical translation. Challenges include adverse nanoparticle interactions with blood components and off-target accumulation in healthy tissues causing toxicity. Scaling up specialized manufacturing and complex functionalization processes for clinical grade therapeutics also remains difficult. Nevertheless, nanotechnology offers disruptive potential in both cervical cancer treatment and diagnosis.

VI. Artificial Intelligence Applications

Artificial intelligence (AI) offers new opportunities to enhance cervical cancer prevention and detection. Machine learning algorithms can analyze patterns in large datasets that surpass human capability [29]. One application is automating Pap smear cytology review. AI can potentially improve efficiency and accuracy of cervical cytology interpretation. But current automated Pap analysis technology still requires ongoing human validation and quality oversight [30]. Other techniques apply predictive modeling and data mining to optimize cervical cancer screening protocols based on risk factors in an individual's health records [31-35]. This supports evidence-based screening guidelines tailored to a woman's characteristics and medical history [36].

AI also shows promise for improving colposcopy and guiding biopsy. Computer vision algorithms can assess digital colposcopy images for lesions and determine optimal biopsy locations. However, real-world clinical validation remains limited [37]. Despite rapid progress, AI still has limitations. Algorithms depend heavily on quality and completeness of input data for model training. They may propagate biases and inherited discrimination present in historical medical data. Transparency regarding data sources, model capabilities, and need for human supervision is critical as AI gains traction in cervical cancer diagnostics.

VII. Personalized Medicine

Advances in molecular profiling and precision oncology are paving the way for more individualized approaches to cervical cancer care [38]. The biological mechanisms linking diabetes to cervical cancer pathogenesis likely involve hyperinsulinemia, chronic inflammation, and immune dysfunction. Hyperinsulinemia may promote cancer cell proliferation, while high blood glucose levels may fuel cancer cell metabolism. Diabetes is also associated with reduced immune surveillance and impaired clearance of human papillomavirus infection, which is causally linked to cervical cancer. Furthermore, women with diabetes tend to have lower cervical cancer screening rates, leading to later stage at diagnosis [39]. Chronic hepatitis C virus (HCV) infection may also increase the risk of cervical neoplasia and cervical cancer [40]. Understanding each patient's unique tumor biology enables customized treatment plans. Pharmacogenomics examines how genetic variation impacts drug metabolism and efficacy. Screening certain pharmacogenes may optimize chemotherapy selection and dosing in cervical cancer. Molecular subtyping also distinguishes prognostic cervical cancer subgroups guiding targeted interventions [41]. Liquid biopsies analyzing circulating tumor cells or cell-free DNA in blood are also gaining traction as minimally invasive approaches for molecular characterization, treatment monitoring, and early relapse detection. These allow longitudinal tracking of an individual's changing tumor genetics [42]. Additionally, research on therapies precisely targeting the specific molecular aberrations driving a patient's cancer continues. Examples include PARP inhibitors for BRCA-mutated tumors and anti-PD-1 immunotherapy for microsatellite unstable cervical cancers [43]. However, numerous barriers exist to translating cervical cancer precision medicine into routine practice. These include inadequate tissue for comprehensive profiling, updating protocols to align with rapidly evolving molecular knowledge, insurance coverage limitations, and managing the increasing complexity of information.

Innovation	Description	Challenges to Translation
HPV DNA Testing	Detect cervical infection with high-risk HPV strains	Optimization of testing protocols and intervals
Liquid-Based Cytology	Suspended cell samples for cytological analysis	Unclear advantage over conventional cytology
Spectroscopy	Tools to analyze cervical tissue biochemical properties	Cost, verification of real-world accuracy
Nanomedicine	Nanoparticles for drug delivery and diagnostics	Toxicity, manufacturing barriers
AI Imaging Analysis	Automated reading of cytology slides and colposcopy	Requires quality data at scale and ongoing oversight

Table 3: innovations in cervical cancer screening and medicine:

VIII. Future directions

Figure 2

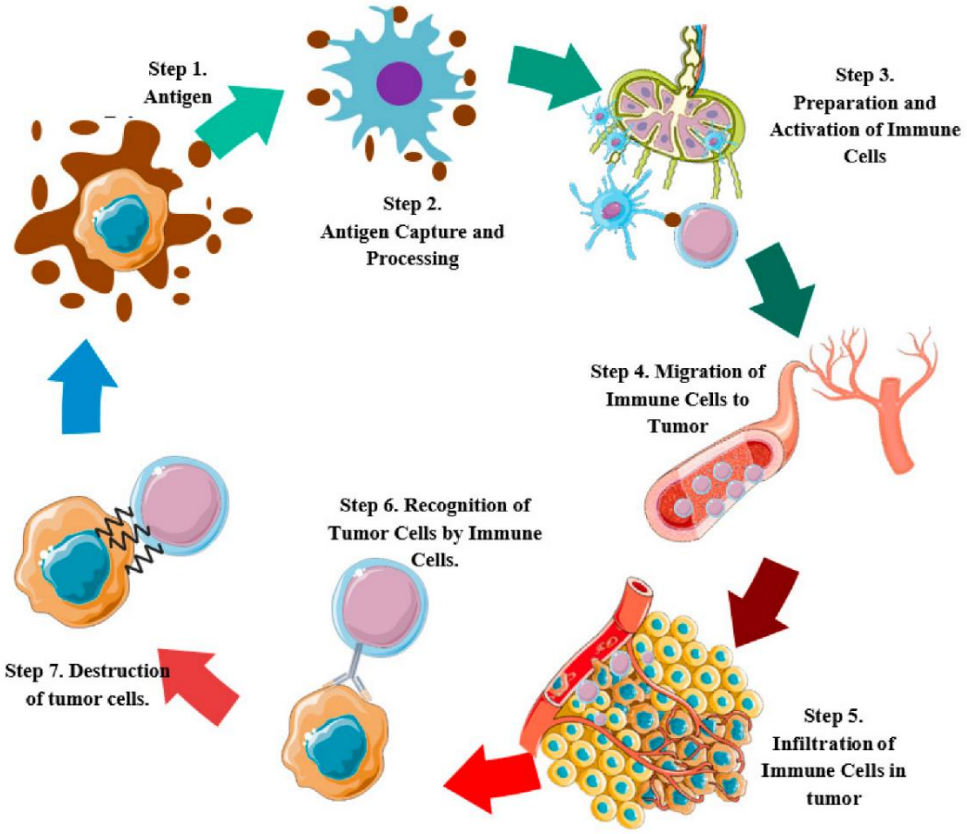

Figure 2. Antitumor Immune Response Mediated by T-Cells [44]

outlines the key stages of the adaptive cellular immune response against tumors. First, antigens are released from dying tumor cells. These antigens are taken up by antigen presenting cells like dendritic cells and macrophages, which process them into peptides (step 2). The antigen presenting cells then migrate to lymph nodes where they prime and activate T-cells by presenting antigens on MHC molecules (step 3). Activated tumor-specific T-cells

proliferate and enter circulation to traffic to the tumor site (steps 4 and 5). Upon infiltrating the tumor, T-cells recognize their target antigens on malignant cells via interaction between their T-cell receptors and MHC-peptide complexes (step 6). Recognition triggers T-cell effector functions leading to direct killing of tumor cells or secretion of cytotoxic molecules like perforin and granzymes (step 7). This T-cell-mediated cytotoxicity is a crucial mechanism of antitumor immunity. Enhancing the specificity and magnitude of T-cell responses through immunotherapy is a promising approach to improve cancer outcomes [44]. Cervical cancer screening is evolving with several changes on the horizon. One major shift will be utilizing HPV DNA testing as the primary screening approach.

Multiple major health organizations already endorse HPV testing alone or in combination with cytology for women over age 30. As evidence continues mounting, HPV testing is likely to replace the Pap smear as the preferred first-line screening modality [45]. Another trend will be combining multiple screening modalities like HPV testing, cytology, and spectroscopy-based technologies. A multimodal approach can integrate the strengths of each method to potentially improve accuracy even further. Automation and computer-assisted interpretation of results may also enhance efficiency and reliability [46]. Expanding access to screening with alternatives like at-home self-sampling will also broaden screening reach. Self-collection models are being implemented, enabling underserved populations to complete simple

HPV tests. Patient compliance may improve with convenient options that fit individual circumstances.

IX. Conclusions

Cervical cancer screening and diagnosis are undergoing an evolution driven by emerging technologies like HPV testing, liquid cytology, spectroscopy, nanomedicine, and artificial intelligence. While the conventional Pap smear

and cervical biopsy remain the most validated screening approaches currently, their dominance is being challenged by innovations that offer enhanced accuracy, convenience, and accessibility. HPV DNA testing as a primary screening modality appears imminent based on accumulating supportive evidence and endorsement by major health organizations. At-home self-collection models are also expanding screening access. However, full displacement of traditional techniques has yet to occur. Most alternatives still lack extensive clinical verification and require standard cytology or biopsy for follow-up of abnormalities. Cost, manufacturing, and regulatory barriers also impede translation of cutting-edge tools like nanodiagnostics. A common theme is that integrating strengths of both established and novel methods through a multimodal screening protocol holds the most promise moving forward. Computer-assisted interpretation may further optimize performance. Emerging frontiers like precision oncology and immunotherapy are advancing cervical cancer treatment. But realizing their potential hinges on resolving challenges like molecular characterization of inadequate biopsy tissue and aligning constantly evolving genomic knowledge with clinical practice. Overall, an era of disruptive change led by technology is dawning in cervical cancer medicine, opening new horizons for detection and management. But thoughtfully leveraging both conventional and innovative approaches during this transition will be key.

X. Recommendations

- HPV testing should be adopted as the primary screening modality for women over age 30, while cytology screening should continue for women under 30. Co-testing with both modalities is optimal for robust detection.

- Efforts to expand screening access through self-sampling options should be accelerated, along with piloting the real-world performance of emerging tools like spectroscopy and nanodiagnostics.

- Computer-assisted interpretation using AI should be implemented to improve efficiency and accuracy of cytology and colposcopy analysis, but requires ongoing quality assurance.

- Treatment guidelines must be continuously updated to integrate precision medicine advances like genomic profiling, molecular subtyping, and targeted therapies based on a tumor's specific aberrations.

- Biobanking of tumor specimens and liquid biopsies should be prioritized to enable comprehensive molecular characterization and longitudinal monitoring for personalized management.

- Patient education on new screening modalities, precancer management, and adherence to follow-up recommendations is paramount.

- Cost-effectiveness assessments and equitable access must be considered in integrating pricey emerging technologies into cervical cancer prevention and care.

- Further research into disruptive innovations like nanotheranostics, immunotherapy, and additional precision medicine approaches should remain a priority.

By pursuing these recommendations, practitioners can optimize integration of proven conventional techniques with promising modern tools to continue advancing cervical cancer medicine and improving patient outcomes.

List of abbreviations

- HPV: Human papillomavirus

- AI: Artificial intelligence

- DNA: Deoxyribonucleic acid

- Pap: Papanicolaou

- PARP: Poly (ADP-ribose) polymerase

- PD-1: Programmed cell death protein 1

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Consent for publication: Not Applicable

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References

1. Chu, Daming, Tengteng Liu, and Yuan Yao. (2023). "Implications of Viral Infections and Oncogenesis in Uterine Cervical Carcinoma Etiology and Pathogenesis." Frontiers in Microbiology 14, (2023): 1194431.
2. Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH. 2019 ASCCP Risk-Based Management Consensus Guidelines Committee. 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. *J Low Genit Tract Dis*. 2020 Apr;24(2):102-131.
3. Kang M, Ha SY, Cho HY, Chung DH, Kim NR. et al. (2020). Comparison of papanicolaou smear and human papillomavirus (HPV) test as cervical screening tools: can we rely on HPV test alone as a screening method? An 11-year retrospective experience at a single institution. *J Pathol Transl Med*.54(1):112-118.
4. Sachan PL, Singh M, Patel ML, Sachan R. (2018). A Study on Cervical Cancer Screening Using Pap Smear Test and Clinical Correlation. *Asia Pac J Oncol Nurs*.5(3):337-341.
5. Nassiri S, Aminimoghaddam S, Sadaghian MR, Nikandish M, Jamshidnezhad N. et al. (2022). Evaluation of the diagnostic accuracy of the cervical biopsy under colposcopic vision. *Eur J Transl Myol*.
6. Chu, Mandy Man-Yee, Charleen Sze-Yan Cheung, Siew-Fei Ngu, Ka-Yu Tse. et al. (2023). "The Value of Four-Quadrant Cervical Biopsy in Women with Different Colposcopic Impressions" Diagnostics 13, no.
7. Addissouky TA, El Tantawy El Sayed I, Ali MMA, Wang Y, El Baz A. et al. (2023). Can Vaccines Stop Cancer Before It Starts? Assessing the Promise of Prophylactic Immunization Against High-Risk Preneoplastic *Lesions J Cell Immunol.*
8. Lellé, R.J., Küppers, V. (2023). Introduction. In: Colposcopy. *Springer*, Cham.
9. Wu, Minxia, and Zhixue You. (2023). "Selective Applications of Excisional Surgical Treatments of Cervical Precancers." *Gynecology and Obstetrics Clinical Medicine* 3, no. 4 (2023): 198-202.
10. Ramírez AT, Valls J, Baena A, Rojas FD, Ramírez K. et al. (2023). Performance of cervical cytology and HPV testing for primary cervical cancer screening in Latin America: an analysis within the ESTAMPA study. Lancet Reg Health Am. 2023 Sep 20;26:100593.
11. Sambyal, Diksha, and Abid Sarwar. (2023). "Recent Developments in Cervical Cancer Diagnosis Using Deep Learning on Whole Slide Images: An Overview of Models, Techniques, Challenges and Future Directions." Micron 173, 103520.
12. Okayama, Kaori, Mao Kakinuma, Saki Tajima, Norika Nagasawa. (2023). "Optimal Papanicolaou Smear Conditions for Manual Microdissection of Single Target Cells" Microorganisms 11, no. 11: 2700.
13. Rayner M, Welp A, Stoler MH, Cantrell LA. (2023). Cervical Cancer Screening Recommendations: Now and for the Future. Healthcare (Basel);11(16):2273.
14. Mustafa WA, Ismail S, Mokhtar FS, Alquran H, Al-Issa Y. (2023). Cervical Cancer Detection Techniques: A Chronological Review. Diagnostics (Basel).13(10):1763.
15. Gibert, M.J., Sánchez-Contador, C. & Artigues, G. (2023). Validity and acceptance of self vs conventional sampling for the analysis of human papillomavirus and Pap smear. Sci Rep 13, 2809.
16. Lee, Yong-Moon, Boreom Lee, Nam-Hoon Cho, and Jae Hyun Park. (2023). "Beyond the Microscope: A Technological

Overture for Cervical Cancer Detection" Diagnostics 13, no. 19: 3079.

17. Olivas, A. D.; Barroeta, J. E.; Lastra, R. R. (2023). Overview of Ancillary Techniques in Cervical Cytology. Acta Cytologica, 67 (2), 119–128.
18. Vahabi, M., Mishra, G., Pimple, S. et al. (2023). Effectiveness of family-centred sexual health education and HPV self-sampling in promoting cervical cancer screening among hard-to-reach indian women in rural and tribal areas: a community-based pilot study. *BMC Public Health*.
19. Addissouky TA, Ali MMA, El Tantawy El Sayed I, Wang Y. (2023). Recent Advances in Diagnosing and Treating Helicobacter pylori through Botanical Extracts and Advanced Technologies. Arch Pharmacol Ther.5(1):53-66.
20. Abd Rashid, Norhashima, Nor Haliza Mohamad Najib, Nahdia Afiifah Abdul Jalil, and Seong Lin Teoh. (2023). "Essential Oils in Cervical Cancer: Narrative Review on Current Insights and Future Prospects" Antioxidants 12.
21. Radovanović, Katarina, Neda Gavarić, and Milica Aćimović. (2023). "Anti-Inflammatory Properties of Plants from Serbian Traditional Medicine" Life 13, no. 4: 874.
22. Oyanna VO, Garcia-Torres KY, Bechtold BJ, Lynch KD, Call MR. et al. (2023). Goldenseal-Mediated Inhibition of Intestinal Uptake Transporters Decreases Metformin Systemic Exposure in Mice. *Drug Metab Dispos*.51(11):1483-1489.
23. Kuck K, Unterholzner A, Lipowicz B, Schwindl S, Jürgenliemk G. et al. (2023). Terpenoids from Myrrh and Their Cytotoxic Activity against HeLa Cells. Molecules. 28(4):1637.
24. Li L, Yang X, Tran D, Seo SK, Lu Y. (2023). Combined Oral Contraceptives As Victims of Drug Interactions. Drug Metab Dispos. 51(6):718-732.
25. Addissouky, T.A., Sayed, I.E.T.E., Ali, M.M.A. et al. (2024). Latest advances in hepatocellular carcinoma management and prevention through advanced technologies. Egypt Liver.
26. Addissouky, T.A., Wang, Y., El Sayed, I.E. et al. (2023). Recent trends in Helicobacter pylori management: harnessing the power of AI and other advanced approaches. *Beni-Suef Univ J Basic Appl Sci* 12.
27. Hong L, Li W, Li Y, Yin S. (2023). Nanoparticle-based drug delivery systems targeting cancer cell surfaces. RSC Adv.13(31):21365-21382.
28. Alrushaid N, Khan FA, Al-Suhaimi EA, Elaissari A. (2023). *Nanotechnology in Cancer Diagnosis and Treatment*. Pharmaceutics. 22;15(3):1025.
29. Razzak MA, Islam MN, Aadeeb MS, Tasnim T. (2023). Digital health interventions for cervical cancer care: A systematic review and future research opportunities. PLoS One.18(12):e0296015.
30. Nakisige C, de Fouw M, Kabukye J, et al. (2023). Artificial intelligence and visual inspection in cervical cancer screening, *International Journal of Gynecologic Cancer Published Online First.*
31. T A Addissouky, A A Khalil, A E El Agroudy. (2023). Assessment of potential biomarkers for early detection and management of Glomerulonephritis patients with diabetic diseases, *American Journal of Clinical Pathology*, Volume 160, Issue Supplement_1, November 2023, Pages S18–S19.
32. T A Addissouky, A A Khalil, A E El Agroudy. (2023). Assessing the Efficacy of a Modified Triple Drug Regimen Supplemented with Mastic Gum in the Eradication of Helicobacter pylori Infection, *American Journal of Clinical Pathology*. Volume 160, Issue Supplement_1, November 2023, Page S19.
33. T A Addissouky, A A Khalil. (2020). Detecting Lung Cancer Stages Earlier By Appropriate Markers Rather Than Biopsy And Other Techniques, *American Journal of Clinical Pathology*, Volume 154, Issue Supplement_1, October. Pages S146–S147.
34. Tamer Addissouky. (2019). Detecting Liver Fibrosis by Recent Reliable Biomarkers in Viral Hepatitis Patients, *American Journal of Clinical Pathology*, Volume 152, Issue Supplement_1, October 2019, Page S85.
35. Addissouky, T.A., Sayed, I.E.T.E., Ali, M.M.A. et al. (2024). Latest advances in hepatocellular carcinoma management and prevention through advanced technologies. Egypt Liver Journal 14.
36. Afaq M, Abraham DE, Patel SH, Al-Dhoon AD, Arshad Z. (2023). Empowering Women's Health: A Global Perspective on Artificial Intelligence and Robotics. Cureus. 15(11):e49611.
37. AlMohimeed, Abdulaziz, Hager Saleh, Sherif Mostafa, Redhwan M. (2023). A. Saad, and Amira Samy Talaat. "Cervical Cancer Diagnosis Using Stacked Ensemble Model and Optimized Feature Selection: An Explainable Artificial Intelligence Approach" Computers 12, no. 10: 200.
38. Begliarzade, Sema, Albert Sufianov, Tatiana Ilyasova, Alina Shumadalova. (2024)."Circular RNA in Cervical Cancer: Fundamental Mechanism and Clinical Potential." Non-coding RNA Research 9, no. 1. 116-124.
39. 34-Addissouky T, Ali M, El Tantawy El Sayed I, Wang Y. (2023). Revolutionary Innovations in Diabetes Research: From Biomarkers to Genomic Medicine. IJDO 2023; 15 (4) :228-242.
40. Addissouky TA, Ali MMA, El Tantawy El Sayed I, Wang Y, El Baz A. et al. (2023). Preclinical Promise and Clinical Challenges for Innovative Therapies Targeting Liver Fibrogenesis. Arch Gastroenterol Res.4(1):14-23.
41. Reizine NM, O'Donnell PH. (2022). Modern developments in germline pharmacogenomics for oncology prescribing. CA Cancer J Clin;72(4):315-332.
42. Addissouky, T.A., Wang, Y., Megahed, F.A.K. et al. (2021). Novel biomarkers assist in detection of liver fibrosis in HCV patients. Egypt Liver.
43. Bhamidipati, D., Haro-Silerio, J.I., Yap, T.A. et al. (2023). PARP inhibitors: enhancing efficacy through rational combinations. *Br J Cancer* 129, 904–916 (2023).
44. Avila, Jonathan Peña, Bruno Melo Carvalho, and Eliane Campos Coimbra. (2023). "A Comprehensive View of the Cancer-Immunity Cycle (CIC) in HPV-Mediated Cervical Cancer and Prospects for Emerging Therapeutic Opportunities" Cancers 15, no. 4: 1333.
45. Tang JH, Lee F, Chagomerana MB, Ghambi K, Mhango P. (2023).Results from Two HPV-Based Cervical Cancer Screening-Family Planning Integration Models in Malawi: A Cluster Randomized Trial. Cancers (Basel).15(10):2797.
46. Hall, M.T., Simms, K.T., Murray, J.M. et al. (2023). Benefits and harms of cervical screening, triage and treatment strategies in women living with HIV. Nat Med 29, 3059–3066.

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