METHODS FOR CERVICAL CANCER SCREENING

MÉTODOS DE RASTREAMENTO PARA O CÂNCER DE COLO UTERINO

MÉTODOS DE DETECCIÓN DEL CÁNCER DE CUELLO UTERINO

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ABSTRACT

Cervical cancer is one of the leading causes of mortality among women in Brazil, with high incidence especially in the Northern region. This chapter addresses the main screening and diagnostic methods for the disease, ranging from conventional cytology to advanced molecular technologies. Liquid-based cytology, HPV DNA and mRNA tests, co-testing, and self-sampling are discussed, as well as the application of biomarkers such as p16INK4a, Ki-67, MCM2, and the methylation of tumor suppressor genes. Detailed comparisons are made based on sensitivity, specificity, cost, and accessibility. The analysis shows that HPV-DNA testing by PCR, with partial genotyping and reflex cytology for positive cases, represents the most cost-effective strategy for implementation in Brazil, combining high diagnostic performance, economic feasibility, and scalability. The adoption of this approach, associated with strategies such as self-sampling, may reduce regional inequalities and promote effective large-scale disease control.

Keywords: Cervical Cancer. HPV. Cytology. Screening. Molecular Tests.

RESUMO

O câncer do colo do útero é uma das principais causas de mortalidade entre mulheres no Brasil, com alta incidência especialmente na região Norte. Este capítulo aborda os principais métodos de rastreamento e diagnóstico da doença, desde a citologia convencional até tecnologias moleculares avançadas. Discutem-se a citologia em meio líquido, os testes de HPV por DNA e mRNA, o co-teste e a auto-coleta, bem como a aplicação de biomarcadores como p16INK4a, Ki-67, MCM2 e a metilação de genes supressores tumorais. Comparações detalhadas são feitas com base em sensibilidade, especificidade, custo e acessibilidade. A análise evidencia que o teste de HPV-DNA por PCR, com genotipagem parcial e citologia reflexa para os positivos, representa a estratégia mais custo-efetiva para implementação no Brasil, conciliando alto desempenho diagnóstico, viabilidade econômica e capacidade de

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ampliação. A adoção dessa abordagem, associada a estratégias como a auto-coleta, pode reduzir desigualdades regionais e promover o controle efetivo da doença em larga escala.

Palavras-chave: Câncer do Colo do Útero. HPV. Citologia. Rastreamento. Testes Moleculares.

RESUMEN
El cáncer de cuello uterino es una de las principales causas de mortalidad entre las mujeres en Brasil, con alta incidencia especialmente en la región Norte. Este capítulo aborda los principales métodos de detección y diagnóstico de la enfermedad, desde la citología convencional hasta tecnologías moleculares avanzadas. Se discuten la citología en medio líquido, las pruebas de HPV por ADN y ARNm, el co-test, y la auto-toma, así como la aplicación de biomarcadores como p16INK4a, Ki-67, MCM2 y la metilación de genes supresores tumorales. Se realizan comparaciones detalladas basadas en sensibilidad, especificidad, costo y accesibilidad. El análisis evidencia que la prueba de HPV-ADN por PCR, con genotipificación parcial y citología refleja para los casos positivos, representa la estrategia más costo-efectiva para su implementación en Brasil, al conciliar alto rendimiento diagnóstico, viabilidad económica y capacidad de expansión. La adopción de este enfoque, asociada a estrategias como la auto-toma, puede reducir las desigualdades regionales y promover el control efectivo de la enfermedad a gran escala.

Palabras clave: Cáncer de Cuello Uterino. HPV. Citología. Detección. Pruebas Moleculares.

1 INTRODUCTION

Cervical cancer is the third most common among women in Brazil (excluding non-melanoma skin cancer), with an estimated 17,010 new cases between 2023 and 2025, and a rate of 15.38 per 100 thousand women. In the North Region, it is the second most frequent, with a rate of 20.48, and Tocantins ranks fourth regionally, with 16.77 cases per 100 thousand (INCA, 2022).

The main cause is HPV infection, especially types 16 and 18, followed by other subtypes such as 31, 33, 35, among others (Williamson, 2023). Vaccination based on the virus's L1 protein is effective, inducing neutralizing antibodies. Children under 16 years of age have a better vaccine immune response than the one obtained naturally (Williamson, 2023).

For secondary prevention, the Pap smear remains the primary method. Liquid collection improves cell conservation and allows HPV genotyping, facilitating the detection of oncogenic subtypes and refining the prognosis (IARC, 2022; MONTEIRO, 2017).

In 2024, the Ministry of Health published SECTICS/MS Ordinance No. 3, incorporating molecular tests with PCR for the detection of oncogenic HPV. While it is not widely implemented, the Pap smear test remains the main method for women aged 25 to 64 years (BRASIL, 2024).

2 MATERIALS AND METHODS

This is a literature review, with a qualitative and descriptive approach, with the objective of identifying and synthesizing the main methods of screening and diagnosis of cervical cancer, covering classic and emerging technologies, such as cytological, molecular and biomarker tests. Data sources included PubMed, Scielo, ScienceDirect, Google Scholar, and official documents from INCA, WHO, and the Ministry of Health.

Studies available in full, in Portuguese, English or Spanish, with the descriptors: cervical cancer, screening, diagnosis and HPV were included. Studies on other gynecological neoplasms, in vitro studies, and publications without methodological clarity were excluded.

The selection was based on thematic relevance and scientific quality. The methodological steps involved reading, critical analysis and categorization of data into topics such as conventional and liquid cytology, HPV tests (DNA/mRNA), co-testing, self-collection and biomarkers. Variables included sensitivity, specificity, cost, and clinical applicability.

3 MAIN CERVICAL CANCER SCREENING TESTS

3.1 CONVENTIONAL CYTOLOGY (PAP SMEAR)

Conventional cytology, or Pap smear, was a milestone in preventive medicine in the twentieth century, reducing mortality from cervical cancer in countries with organized screening programs (CHANDRASEKHAR; KRISHNAMURTI, 2018; BHATLA; SINGHAL, 2020; LONGATTO-FILHO et al., 2015). The exam analyzes exfoliated cells from the cervix, identifying dysplastic or neoplastic changes early.

George Papanicolaou began his studies in the 1920s, but it was in 1941, with Herbert Traut, that he published the work that consolidated the technique. Since then, the test has gained recognition for its effectiveness in the early detection of cervical cancer (CHANDRASEKHAR; KRISHNAMURTI, 2018).

The collection is done in the transformation zone, a region susceptible to HPV infection, with an Ayre spatula and an endocervical brush. The cells are fixed on a slide with ethanol or a specific fixative and stained with the Pap smear technique, which differentiates nuclei and cytoplasm according to the degree of keratinization (FREITAS et al., 2023; ALENCAR et al., 2021).

Interpretation is performed by cytotechnicians and pathologists, based on cellular morphological changes. Findings are classified according to the Bethesda System, which standardizes diagnoses, including categories such as ASC-US, LSIL, HSIL, and AIS (SMITH et al., 2018; WILLIAMS et al., 2022). Although specific, the test has variable sensitivity (30% to 87%) and a false negative rate between 14% and 33% (FREITAS et al., 2023). The quality of the collection and reading directly influences the results. Periodic repetition and laboratory control are recommended (BHATLA; SINGHAL, 2020).

In Brazil, the SUS offers the test, but coverage is unequal, with greater adherence in the Southeast and South. Opportunistic screening leads to duplication in some women and absence in others, making it difficult to reduce mortality, especially in more vulnerable regions (SILVA et al., 2023).

3.2 CYTOLOGY IN LIQUID MEDIUM (LBC)

Liquid-Based Cytology (LBC) represents a technical advance that aims to overcome limitations of conventional cytology (IARC, 2022). In this approach, after collection with an endocervical brush, the cellular material is transferred to a flask containing a preserving medium, where it is suspended and processed in the laboratory by automated filtration or sedimentation methods (FREITAS et al., 2023; LONGATTO-FILHO et al., 2015). The final

preparation results in a slide with a cellular monolayer, reducing overlap and artifacts (MONTEIRO, 2017).

In addition to improving the morphological quality of the slides, the LBC allows sample reuse for additional tests such as HPV DNA/mRNA detection, viral genotyping, screening for STIs (chlamydia, gonorrhea), and immunocytochemical or molecular analyses. (FREITAS et al., 2023). Studies such as the one by LONGATTO-FILHO et al. (2015) point out that AML reduces unsatisfactory smears from 3% to 0.3%, improves the detection of LSIL and HSIL, and allows integration with automated cytological screening platforms.

In practice, AML improves diagnostic yield and optimizes the use of laboratory resources. However, the high initial cost of both the preservative medium and the equipment limits its universalization in public health systems. For its large-scale implementation, it is necessary to invest in laboratory infrastructure, technical training and cost-effectiveness assessment.

3.3 DNA TYPING

DNA typing of the human papillomavirus (HPV) is a fundamental technique in screening and risk stratification for cervical cancer. Its main purpose is to identify the presence of oncogenic HPV types, especially high-risk ones, such as HPV-16, 18, 31, 33, among others. This method is based on the detection and amplification of specific sequences of viral DNA by molecular biology techniques, the most used being Polymerase Chain Reaction (PCR) and Hybrid Capture (WILLIAMS et al., 2022; BHATLA; SINGHAL, 2020).

3.4 PCR (POLYMERASE CHAIN REACTION)

PCR is a technique for enzymatic amplification of DNA segments. In the context of HPV, it allows the detection of small amounts of the viral genetic material present in cells collected from the cervical epithelium. Using specific primers for conserved regions of the HPV genome (such as the L1, E6, and E7 genes), PCR can identify the presence of the virus, quantify its viral load, and even determine the viral genotype when combined with specific probes or subsequent sequencing (WILLIAMS et al., 2022).

Real-time PCR (qPCR) allows the quantification of viral load in real time, and is useful in clinical research to assess the persistence of infection and its association with the progression of lesions (HAWKINS; GUEST, 2016). Multiplex PCR, on the other hand, allows the simultaneous detection of multiple HPV genotypes in a single reaction, optimizing time and resources (HAWKINS; GUEST, 2016; BHATLA; SINGHAL, 2020).

3.5 HYBRID CAPTURE®

The hybrid capture technique uses RNA probes that hybridize with the viral DNA present in the sample, forming an RNA-DNA complex later detected by chemiluminescence. This approach makes it possible to distinguish between infections caused by high- and low-risk HPV types, and is applied in commercial tests such as Hybrid Capture 2®, approved by regulatory bodies such as the FDA (POLJAK et al., 2009; ADORNO et al., 2020).

In addition to its consolidated clinical applicability, studies indicate that this methodology has greater sensitivity compared to conventional cytology, especially in the detection of high-grade intraepithelial lesions. As demonstrated in the analysis of hybrid captures for HPV in women with cervical intraepithelial lesion (2025), the test is able to identify suspected cases of CIN 2 and CIN 3 with a performance of more than 95%, reinforcing its usefulness in the early identification of precursor alterations of cervical cancer.

In addition, the gradual incorporation of this method into screening programs has been associated with a significant reduction in invasive cervical cancer rates in subsequent screening cycles (ADORNO et al., 2020).

3.6 VAGINAL SELF-COLLECTION FOR HPV-DNA TESTING

Self-collection is a strategy that aims to expand cervical cancer screening coverage, especially among women who face geographical, social, or cultural barriers to accessing health services (EUN; PERKINS, 2020). The technique consists of using devices such as cervicovaginal swabs, soft brushes, or vaginal washes, which can be applied by the woman herself at home or in community settings (NISHIMURA et al., 2021).

Studies have shown that the sensitivity of self-collection for HPV detection is comparable to clinical collection performed by professionals, provided that the technique is correctly performed and the molecular analysis method is validated (such as PCR or hybrid capture). The World Health Organization (WHO) recognizes self-collection as an effective alternative, especially in low-coverage contexts (NISHIMURA et al., 2021; EUN; PERKINS, 2020).

The most commonly used devices include:

- Sterile swab: similar to the one used for oropharyngeal collection, it allows obtaining cells from the vaginal fundus and ectocervix;
- Cervical brush (cervibrush): it has soft bristles designed for collecting the squamocolumnar junction;
- Lavage device: consists of the introduction of a sterile solution that is collected after contact with the vaginal and cervical epithelium (NISHIMURA et al., 2021).

To ensure diagnostic accuracy, it is essential to provide clear guidance and illustrative materials about the procedure, as well as to ensure proper transportation of the sample to the laboratory. The acceptance of self-collection among women is high, mainly because it provides greater privacy, comfort, and autonomy in health care (NISHIMURA et al., 2021).

Integrating self-collection into national screening programs can significantly contribute to reducing inequalities in access and improving early detection indicators, particularly in low-income regions or remote areas (IARC, 2022).

3.7 CO-TEST: LIQUID CYTOLOGY ASSOCIATED WITH HPV TEST

Co-testing is a screening strategy that combines cytology and molecular detection of high-risk HPV in a single collection. This allows the evaluation of cell morphology and the identification of the etiological agent simultaneously, with greater diagnostic sensitivity and less chance of screening failures (NUE; PERKINS, 2020; JANS et al., 2021).

Preferably performed with liquid cytology (LBC), the method allows the preparation of cytological slides and the use of residual material for molecular tests, such as PCR or hybrid capture. This approach is feasible due to the stability of nucleic acids in the liquid medium (EUN; PERKINS, 2020; MONTEIRO, 2017; LONGATTO-FILHO et al., 2015).

Studies show that co-testing is effective in detecting HSIL and AIS, particularly in women at higher risk. Cytology, despite its good specificity, has limited sensitivity (53%), while the HPV test, which is more sensitive, has lower specificity, especially in young women (BHATLA; SINGHAL, 2020; CARVALHO et al., 2022). The association aims to balance these limitations.

Although co-testing increases the detection of CIN2+ and CIN3+, this may reduce specificity. Compared with HPV testing alone, additional benefits are limited, and a negative HPV test is already considered reliable in excluding significant lesions (BHATLA; SINGHAL, 2020; EUN; PERKINS, 2020; NORDQVIST KLEPPE et al., 2023; CARVALHO et al., 2022).

From an economic point of view, co-testing requires more tests and colposcopies, increasing costs to detect few additional cases. The WHO indicates that the harms — such as unnecessary referrals — can outweigh the benefits, making their use restricted to specific contexts (JANS et al., 2021; BHATLA; SINGHAL, 2020; NORDQVIST KLEPPE et al., 2023; EUN; PERKINS, 2020).

3.8 MRNA TESTING (APTIMA)

The APTIMA® test (Hologic Inc.) detects mRNA from HPV genes E6 and E7, markers of viral oncogenic activity, differing from DNA tests in indicating biologically active infection

and increased risk of progression to HSIL or cervical cancer (WILLIAMS et al., 2022; BHATLA; SINGHAL, 2020).

This specificity reduces false positives and unnecessary colposcopies (ZHANG et al., 2022). The sample is collected with an endocervical brush and stored in a proper medium (APTIMA® Transfer Medium). The RNA is then amplified by Transcription-Mediated Amplification (TMA), a sensitive isothermal technique (HOLOGIC INC., 2022).

Detection occurs by chemiluminescence with specific probes and automated reading in the Panther® system, providing qualitative or quantitative results (HEIDEMAN et al., 2013).

Studies point to sensitivity similar to that of DNA tests and superior specificity in detecting HSIL, allowing better screening of HPV-positive women (ZHANG et al., 2022). Therefore, it is recommended as a second step after a positive DNA test or as a primary method in systems with good laboratory infrastructure.

Despite the high cost and limitation in low-income countries, APTIMA® stands out as a modern and accurate tool, with the potential to reduce invasive procedures and unnecessary expenses.

3.9 MOLECULAR BIOMARKERS AND EMERGING TECHNIQUES

In order to differentiate transient infections from conditions at risk of progression to invasive neoplasms in HPV-positive women, several biomarkers have been evaluated.

3.10 P16INK4A

p16INK4a is a CDK inhibitor that, in response to cell cycle dysregulation promoted by oncogenic HPV, becomes overexpressed. Its detection by immunohistochemistry is used to confirm high-grade intraepithelial lesions (HSIL) (WILLIAMS et al., 2022; SAVONE et al., 2016).

3.11 KI-67

Present in dividing cells, Ki-67 is useful when expressed in superficial layers of the epithelium, suggesting oncogenic infection (DOEBERITZ, 2025). Double staining with p16 (dual staining, such as CINtec® PLUS Cytology) increases diagnostic accuracy and can avoid unnecessary colposcopies (MIMICA et al., 2010).

3.12 MCM2

The MCM2 protein, expressed on proliferative cells, is increased in neoplastic lesions and cervical cancer (LU et al., 2021; SUN; CHENG; LIU, 2022). Its use in liquid cytology expands its application in population screenings (DEL MORAL-HERNÁNDEZ et al., 2021).

3.13 TOP2A

Topoisomerase II alpha is indirectly regulated by HPV16 via suppression of miR-320a, promoting cell proliferation (ZHANG et al., 2024). Combined with MCM2, in ProEx™ C staining, it demonstrates efficacy in detecting high-grade precursor lesions (PEŠUT et al., 2021; DEL MORAL-HERNÁNDEZ et al., 2021).

3.14 CYCLIN E1

Cyclin E1, encoded by the CCNE1 gene, promotes the G1-S transition. Its overexpression is related to the persistence of HPV and the advancement of cervical lesions, and can be used in conjunction with other biomarkers to improve diagnosis (DEL MORAL-HERNÁNDEZ et al., 2021; ZHAO et al., 2018).

3.15 METHYLATION OF TUMOR SUPPRESSOR GENES

Hypermethylation of genes such as CCNA1, CADM1, and DAPK1 is present from precursor lesions to invasive cancer (YANATATSANEEJIT et al., 2020). Tests such as QIAsure® and GynTect® apply this approach, including in self-collections (BURDIER et al., 2024; BHATLA; SINGHAL, 2020).

3.16 DIGITAL PCR DROPLET (DDPCR)

ddPCR enables accurate quantification of viral load and detection of circulating tumor DNA, being promising in post-treatment follow-up and identification of recurrences (WILLIAMS et al., 2022).

3.17 NEXT GENERATION SEQUENCING (NGS)

NGS allows detection of multiple HPV types and sublineages associated with higher oncogenic risk, with performance comparable to commercial tests such as Cobas®4800 (MÜHR et al., 2021; ANDERSEN et al., 2022). Despite its potential, it still faces logistical and financial challenges.

Clinical implementation of these biomarkers requires large-scale validation and cost-effectiveness analyses, but represents an important advance in screening accuracy and clinical targeting.

Table 1

Comparison between diagnostic methods based on the main characteristics researched

Method	Sensitivity	Specificity	Cost	Accessibility	Test Phase
Conventional Cytology	Moderate (50–75%)	High (86–100%)	Low	High – available in basic services	Widely used
Liquid Cytology (LBC)	Moderate-High (65–85%)	High	Moderate	Moderate – requires structured laboratory	Used
HPV-DNA testing	High (>90%)	Moderate	Low	Low – suitable for few features	Implemented in programs
mRNA Testing (APTIMA)	High (90–95%)	High	High	Low – available in few specialist centres	Restricted clinical use
Co-test (LBC + HPV)	Very High (>95%)	High	High	Low – requires integrated cytology + molecular biology framework	Established clinical use in some countries
p16INK4a	High (85–95%)	Moderate	Low	High – used in routine pathological anatomy	Widely validated
Ki-67 (Dual Stain)	High (90%)	High	Moderate	Moderate – depends on advanced immunocytochemistry	Validated
MCM2	High (80–90%)	Moderate	Moderate	Moderate – requires cytological laboratory with molecular capacity	Under evaluation
TOP2A	Moderate	Moderate	Moderate	Moderate – requires antibodies and expert interpretation	Under evaluation
Cyclin E1	Moderate-High	Moderate	Moderate	Low – use restricted to research centers	In research
Gene Methylation	High (90%)	High	High	Low – available at research centers and pilots	In validation

ddPCR	Very high (>95%)	High	High	Very Low – limited to academic and research environment	Experimental
NGS	High	High	Very High	Very Low – restricted use, high cost and complexity	Experimental

Source: authors.

Table 2

Main positive and negative points of each diagnostic method

Method	Main Positive Points	Main Negative Points
Conventional Cytology	Low cost, good specificity, widely available	Low sensitivity, high false negative rate, dependent collection
Liquid Cytology (LBC)	Improved sample quality, allows for additional testing, lower rate of unsatisfactory slides	Higher cost than conventional costs, requires infrastructure and training
HPV-DNA testing	High sensitivity, identifies infection before injury, good negative predictive value	Low specificity can lead to unnecessary tests, false-positives in young people
mRNA Testing (APTIMA)	High specificity, identifies active infection, reduces unnecessary colposcopies	High cost, less accessibility, demand specialized laboratory
Co-test (LBC + HPV)	Higher sensitivity and negative predictive value, allows extension of the screening interval	High cost, complex laboratory infrastructure, difficult universal implementation
p16INK4a	Validates HSIL, well-established technique, easy integration with histopathology	Limited specificity in isolation, interpretation may vary
Ki-67 (Dual Stain)	Sensitive and specific for high-grade cervical lesions (CIN2+)	Requires dual staining and specific equipment, moderate cost
MCM2	Good proliferation marker, applicable in liquid cytology	Still in broad evaluation, not widely available
TOP2A	Indicates progression of cervical injury to more advanced stages, useful in combinations	Requires expert interpretation, limited use
Cyclin E1	Related to genomic instability, it may increase diagnostic accuracy	Few clinical studies, not validated for primary screening
Gene Methylation	Differentiates regressive from progressive lesions, useful in HPV-positive	High cost, ongoing validation, low availability
ddPCR	Ultra-sensitive quantification, useful in monitoring and viral load	Expensive and research-restricted technology, without broad standardization

NGS	Detects mutations, genotyping, and broad epigenetic profiles	Very expensive and complex, need for bioinformatics, restricted to research

Source: authors.

4 DISCUSSION

Given the wide variety of methods available for cervical cancer screening, the choice of the most appropriate strategy in countries such as Brazil should take into account not only diagnostic performance, but also factors such as cost, accessibility, laboratory infrastructure, and population adherence. In this scenario, it is essential to prioritize approaches that reconcile high sensitivity, logistical feasibility, and cost-effectiveness.

Conventional cytology, although low-cost and widely offered by the SUS, has limited sensitivity (30–87%) and a high rate of false negatives (FREITAS et al., 2023; BHATLA; SINGHAL, 2020). Liquid cytology improves technical aspects and allows multiple tests from the same sample, but its cost and need for infrastructure limit universalization (LONGATTO-FILHO et al., 2015; MONTEIRO, 2017).

The co-test (AML + HPV test) stands out for its very high sensitivity (>95%) and high negative predictive value, being effective in the early detection of HSIL and AIS. However, its high cost and complex laboratory demand make it unfeasible for large-scale implementation in the Brazilian public health system (CARVALHO et al., 2022; NORDQVIST KLEPPE et al., 2023).

Among the approaches based on viral detection, HPV-DNA testing with partial or extended genotyping by PCR is the most appropriate as primary screening. This technique has a sensitivity of more than 90%, good standardization, and moderate cost when compared to other molecular techniques (WILLIAMS et al., 2022; POLJAK et al., 2009). Among the typing methods, PCR with specific probes for types 16 and 18 is the most cost-effective, as it allows the direct identification of genotypes with the highest oncogenic risk and appropriately directs the referral flows for colposcopy (HAWKINS; GUEST, 2016; BHATLA; SINGHAL, 2020). Hybrid capture, although robust, is less specific and does not provide detailed genotypic information, which limits its usefulness in personalized screening strategies (ADORNO et al., 2020). Some authors present a minimal difference in sensitivity (<0.02%) between co-testing and HPV-DNA typing, demonstrating the safety of using screening alone as a screening method. (NORDQVIST KLEPPE et al., 2023).

In addition, the possibility of using vaginal self-collection with HPV-DNA testing by PCR represents a promising alternative to expand access to screening in vulnerable populations, with sensitivity similar to clinical collection and good acceptance by users (EUN; PERKINS, 2020; NISHIMURA et al., 2021).

The mRNA test (APTIMA) emerges as a promising alternative, especially due to its high specificity, as it detects only active infections with a real risk of progression to high-grade neoplasms (WILLIAMS et al., 2022; ZHANG et al., 2022). Its application can be especially useful as a complementary screening test in HPV-positive women with negative cytology, reducing unnecessary referrals for colposcopy (HEIDEMAN et al., 2013; BHATLA; SINGHAL, 2020). However, factors such as high cost, lower availability in the SUS, and the need for equipped laboratories still restrict its large-scale implementation in Brazil (HOLOGIC INC., 2022; EUN; PERKINS, 2020).

Molecular biomarkers and emerging techniques, such as the detection of p16/Ki-67, MCM2, gene methylation, ddPCR, and NGS, represent significant advances in diagnostic refinement (DEL MORAL-HERNÁNDEZ et al., 2021; VON KNEBEL DOEberitz, 2025; BURDIER et al., 2024). These tools offer greater accuracy in identifying high-grade lesions among HPV-positive women, aiding in clinical decision-making and reducing unnecessary interventions (DOEBERITZ, 2025; SAVONE et al., 2016; MÜHR et al., 2021). However, the need for large-scale validation, high costs, and specialized infrastructure still limit its incorporation into population screening programs (BHATLA; SINGHAL, 2020; YANATATSANEEJIT et al., 2020). Despite this, its future adoption, in a selective and integrated manner, can contribute to personalizing screening and improving clinical outcomes (PEŠUT et al., 2021; ANDERSEN et al., 2022).

5 FINAL CONSIDERATIONS

Therefore, primary screening with HPV-DNA testing by PCR (partial genotyping) is recommended as an ideal strategy for Brazil, associated with reflex cytology in positive cases, preferably using samples collected in liquid medium. This approach offers the best balance between clinical performance, economic and operational feasibility, in addition to allowing longer intervals between exams, rationalizing the resources of the health system. Its full adoption may represent a decisive step towards reducing the incidence and mortality from cervical cancer in Brazil in an equitable and sustainable way.

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