СКРИНИНГОВАЯ ИЛИ УГЛУБЛЕННАЯ ЦИТОДИАГНОСТИКА: МЕТОДОЛОГИЧЕСКИЕ РАЗЛИЧИЯ

Научная статья

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Аннотация

В статье рассмотрены методологические различия между скрининговой и углубленной цитодиагностикой. Показано, что скрининговый подход ориентирован на массовое выявление клеточных изменений у лиц без выраженной клинической симптоматики, в то время как углубленный анализ направлен на уточнение морфологической природы процесса, оценку риска злокачественности и выбор дальнейшей диагностической тактики. Раскрыты возможности и ограничения цитологического скрининга злокачественных новообразований. Отдельное внимание уделено факторам, которые влияют на результативность скрининговых программ. Представлен сравнительный анализ скрининговой и углубленной цитодиагностики, а также схема выбора диагностического подхода.

Ключевые слова: цитодиагностика, цитология, скрининг, жидкостная цитология, Bethesda, cell-block, молекулярное тестирование, злокачественные новообразования.

SCREENING OR ADVANCED CYTODIAGNOSTICS: METHODOLOGICAL DIFFERENCES

Research article

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Abstract

The article examines the methodological differences between screening and advanced cytodiagnostics. It is shown that the screening approach is focused on the mass detection of cellular changes in individuals without pronounced clinical symptoms, whereas advanced analysis is aimed at clarifying the morphological nature of the process, assessing the risk of malignancy, and selecting further diagnostic tactics. The possibilities and limitations of cytological screening for malignant neoplasms are discussed. Special attention is paid to the factors that influence the effectiveness of screening programs. A comparative analysis of screening and advanced cytodiagnostics is presented, along with a scheme for selecting a diagnostic approach.

Keywords: cytodiagnostics, cytology, screening, liquid-based cytology, Bethesda, cell block, molecular testing, malignant neoplasms.

Introduction

Cytological diagnostics occupies a distinct place in oncological practice, as it enables the evaluation of cellular material prior to comprehensive morphological examination. In clinical settings, this method is applied in both screening and advanced modes, with screening cytodiagnostics aimed at detecting suspicious cellular abnormalities in large population groups, whereas advanced cytodiagnostics is employed when clinical, instrumental, or laboratory indications justify a more detailed analysis of the specimen. The distinction between these approaches is determined by the purpose of the investigation, the acceptable level of diagnostic uncertainty, and the nature of subsequent clinical decisions, since in mass screening key considerations include population coverage, the feasibility of repeat testing, rapid processing of specimens, and the provision of a clear pathway for further patient evaluation. In contrast, advanced analysis prioritizes morphological accuracy, detailed assessment of cellular composition, and refinement of clinical data, often with the possibility of applying additional diagnostic methods. The most extensively studied model of cytological screening remains cervical cancer prevention, and in countries with high population coverage and effective quality control, cytological screening has led to a substantial reduction in both incidence and mortality, although its effectiveness is highly dependent on program organization, personnel training, and the quality of laboratory procedures [1].

The aim of the study is to conduct a comparative analysis of screening and advanced cytodiagnostics, to determine the indications for an advanced analytical approach, and to

reveal the factors that influence the effectiveness of screening programs for malignant neoplasms.

Materials and methods

The study was conducted in the format of an analytical review of scientific publications on cytological screening, liquid-based cytology, standardized systems of cytological reporting, and additional methods for the analysis of cytological material. The review included articles reflecting the practical effectiveness of screening programs, the diagnostic accuracy of cytology, the impact of laboratory workload, and the significance of advanced technologies.

During the analysis of the sources, two levels of result interpretation were distinguished: the cytological level, based on Bethesda terminology, and an additional risk-oriented level associated with the use of HPV testing [2]. For the description of cytological results, the following Bethesda categories were used: NILM, ASC-US, ASC-H, LSIL, HSIL, AGC, AIS, and malignant changes. HPV testing was considered as an additional method for assessing biological risk and for patient triage, which makes it possible to avoid conflating cytological Bethesda categories with histological classifications of cervical intraepithelial neoplasia.

Results and discussion

Screening cytodiagnostics is implemented based on the principle of early detection of cellular changes before the onset of pronounced clinical manifestations. The purpose of diagnostics in this context is to identify a group of patients who require further examination; therefore, the screening report should be concise, standardized, and suitable for subsequent referral of the patient to specialists.

Advanced cytodiagnostics is applied in the presence of an identified lesion, a questionable screening result, a discrepancy between clinical and cytological findings, suspicion of a neoplastic process, or when it is necessary to determine further treatment strategy. In this context, the cytologist evaluates a set of cellular characteristics, including smear structure, background, atypia, nuclear changes, cellular groupings, and features of degeneration, inflammation, and neoplastic transformation.

In particular, the methodological difference between the considered diagnostic approaches is evident when comparing conventional and liquid-based cytology. M. Arbyn et al., in a systematic review, demonstrated that liquid-based cytology does not always surpass the conventional smear in terms of sensitivity and specificity; however, it offers organizational advantages due to the standardization of specimen preparation and the

possibility of further use of residual material [3]. Therefore, the value of the technology is determined both by the method of specimen preparation and by the role of the method within the diagnostic pathway. In addition, an important condition for the effectiveness of both approaches is a unified language of cytological reporting. The Bethesda system for cervical cytology demonstrates the importance of standardizing terminology, diagnostic categories, and clinical recommendations. For example, R. Nayar and D.C. Wilbur rightly emphasize that a standardized cytological report links laboratory assessment with subsequent clinical actions, thereby reducing the risk of arbitrary interpretation of the result [4]. However, the effectiveness of screening in practice depends on the organization of laboratory work, since even in the presence of a standardized classification, the risk of errors associated with a high volume of specimens remains. In their study, T.M. Elsheikh et al. showed that an increase in cytotechnologist workload above 100 specimens per day in the automated ThinPrep system was associated with a decrease in screening accuracy [5]. Thus, the quality of mass screening is determined, among other factors, by laboratory performance.

In addition, the diagnostic accuracy of cytology also depends on the interpretation threshold; for example, J.S. Pyo et al., in a review of the accuracy of cytology in squamous intraepithelial lesions and cervical cancer, concluded that the results vary depending on the diagnostic category, the type of specimen, and the population under study [6]. For screening, such variability implies the need for continuous quality control; in the case of advanced diagnostics, the emphasis is placed on clinicomorphological correlation. When comparing the two diagnostic approaches, the following differences can be identified (Table 1):

Table 1 – Comparative characteristics of screening and advanced cytodiagnostics

Criterion of comparison	Screening cytodiagnostics	Advanced cytodiagnostics
Primary objective	Detection of suspicious cellular abnormalities in a large examined population	Clarification of the morphological nature of the process
Clinical situation	Preventive examination, routine check-ups, mass screening programs	Questionable result, clinical suspicion, identified lesion
Requirements for the report	Conciseness, standardized category, clear patient routing	Detailed interpretation taking into account cellular composition and clinical data
Acceptable level of uncertainty	Relatively higher, as the result determines the direction of	Lower, since the report influences diagnostic and

	further examination	treatment strategy
Main risk	False-negative or false-positive screening result	Error in the interpretation of complex or limited material
Role of additional methods	Limited, depends on the screening program	Significant, with emphasis on cellular diagnostics, immunomarkers, and molecular testing
Final significance	Selection of patients for further diagnostics	Clarification of the diagnostic category and clinical risk

Indications for an advanced approach arise in three groups of situations:

1) associated with a doubtful or borderline cytological report;
2) formed in the presence of a discrepancy between cytological findings and clinical or instrumental data;
3) related to specimens requiring clarification of the nature of the tumor, the origin of the cells, or molecular characteristics.

An example of a standardized advanced approach is the Bethesda System for Reporting Thyroid Cytopathology. In the 2023 edition, the system retains six diagnostic categories and links each of them with the risk of malignancy and subsequent patient management strategy [7]. Thus, advanced cytodiagnostics makes it possible to determine a diagnostically significant risk category.

In turn, additional methods expand the possibilities of using cytological material. Thus, in their study, S.M. Knoepp and M.H. Roh showed that direct aspiration smears can be used for a range of ancillary studies [8], which is important in cases of limited material volume, when a repeat invasive procedure is undesirable or technically difficult. At the same time, cell blocks allow the performance of special stains, immunohistochemical reactions, and molecular studies on cytological material [9]. Molecular testing enhances the role of cytology in personalized oncology and makes it possible to increase the sensitivity and specificity of diagnostics [10].

In practice, the choice between screening and advanced cytodiagnostics should be determined by the diagnostic task at hand, since the same cytological material may have different value depending on the clinical question (see Fig. 1):

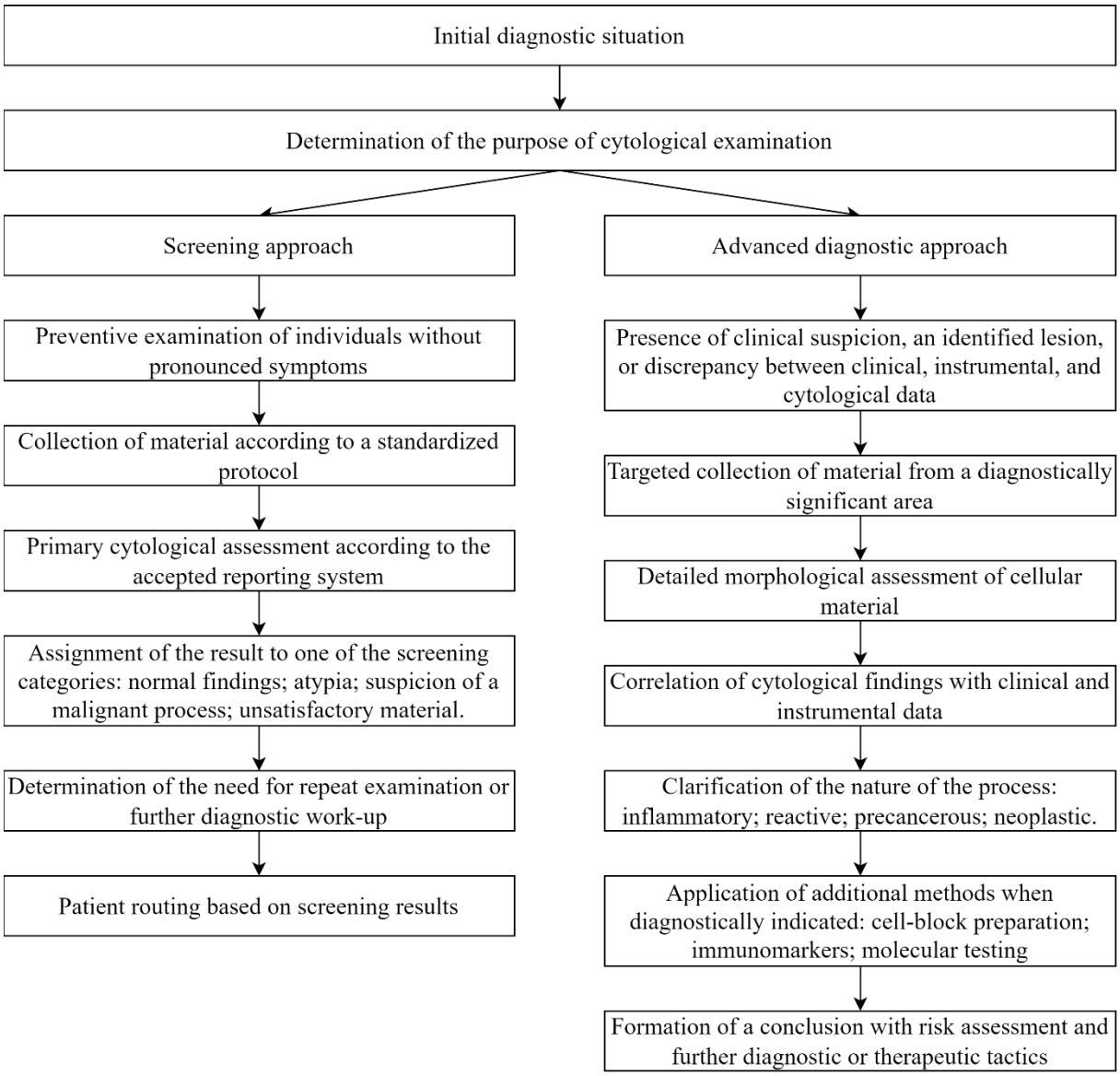


Fig. 1. Scheme for selecting a screening or advanced cytodiagnostic approach

Based on Fig. 1, screening and advanced cytodiagnostics should not be considered equivalent methods for solving the same task, since screening operates at the level of population-based selection, whereas advanced analysis ensures a more accurate establishment of an individual diagnosis. Errors arise in cases where a screening report is interpreted as a final diagnosis, or when advanced investigation is attempted to be replaced by mass screening without consideration of the clinical context.

Conclusion

The conducted study makes it possible to clarify that screening and advanced cytodiagnostics differ in their purpose, methodology, level of detail, and clinical implications of the report. The screening approach is aimed at the mass detection of suspicious cellular abnormalities and requires a high level of standardization at all stages; at the same time, its

effectiveness depends on the coverage of the target population, laboratory quality control, specialist workload, and proper integration of cytology with other methods of early detection of malignant neoplasms. Advanced cytodiagnostics, in turn, is applied in situations where it is necessary to clarify the morphological nature of the process, explain discrepancies between clinical and laboratory data, assess the risk of malignancy, or prepare material for additional studies. The methodological basis of such diagnostics is associated with a detailed assessment of cellular material, standardized diagnostic categories, and the use of cell blocks, immunomarkers, and molecular tests. In other words, screening answers the question of whether further examination is required, whereas advanced cytodiagnostics answers the question of the nature of the detected process and the likely clinical decision.

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