

Role of Biochemical Markers in Early Detection and Prognostication of Cancer Pathology: A systemic Review

Dr.E.Krithiga^{1***}, Dr.Sasikala Gunasekaran², Panneerselvam Periasamy³

1. Dr.E.Krithiga, Assistant Professor, Department of Pathology, Government Erode Medical college, Perundurai, Erode, Tamilnadu. Email: elankiru@gmail.com
2. Dr.Sasikala Gunasekaran, Staff Nurse, Government Erode Medical College Hospital, Perundurai, Erode, Tamilnadu, India. Email: saipannsasi@gmail.com
3. Panneerselvam Periasamy, Assistant Professor, Department of Physiology, Government Erode Medical college, Perundurai, Erode, Tamilnadu. Email: pannphysio@gmail.com

*****Corresponding Author: Dr.E. Krithiga, Email: elankiru@gmail.com**

Received: 08-04-2022 / Revised: 13-05-2022 / Accepted: 01-06-2022

Abstract:

The use of biochemical markers has revolutionized the field of oncology, offering invaluable tools for early cancer detection, monitoring treatment response, and predicting prognosis. This paper delves into the significance of various biochemical markers in cancer pathology, focusing on prostate-specific antigen (PSA), prostatic acid phosphatase (PAP), CA 125, carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), CA 19-9, CA 15-3, CA 27-29, lactate dehydrogenase (LDH), and neuron-specific enolase (NSE).

Keywords: Biochemical Markers, Early Detection, Prognostication, Cancer Pathology

Introduction

Disease stays a main source of bleakness and mortality internationally. Early location and precise anticipation are significant for powerful administration and worked on persistent results. Biochemical markers act as harmless devices that guide in the ID, observing, and comprehension of malignant growth pathologies [1]. Disease stays a considerable worldwide wellbeing challenge, applying a huge cost for people and medical care frameworks around the world. Its perplexing and complex nature requests creative methodologies for early discovery, exact conclusion, and compelling treatment. In this unique situation, biochemical markers have arisen as crucial apparatuses, offering significant bits of knowledge into disease pathology, helping with early recognition, guess, and remedial observing [2]. The mission for recognizing dependable biomarkers has been a foundation of oncological exploration. These markers, frequently proteins

or different substances delivered by disease cells or because of their presence, act as quantifiable signs of physiological or obsessive cycles related with malignancies [3]. Their importance lies in their true capacity for early recognition as well as in directing treatment choices and surveying sickness movement.

This paper expects to investigate the urgent pretended by a few laid out biochemical markers in the domain of malignant growth pathology. The conversation will zero in on explaining the meaning of markers, for example, public service announcement, PAP, CA 125, CEA, AFP, HCG, CA 19-9, CA 15-3, CA 27-29, LDH, and NSE. Every one of these markers holds special significance across various sorts of malignant growth, adding to early analysis, forecast assurance, and treatment checking. Moreover, while these biomarkers have enormously added to malignant growth the executives, challenges continue in regards to their explicitness, awareness, and normalization [4]. Continuous exploration tries look to address these impediments and investigate novel biomarkers that might actually change disease diagnostics and the board.

Understanding the job of biochemical markers in disease pathology is pivotal for medical services specialists, analysts, and patients. Their combination into clinical practice requests a thorough assessment of their assets, restrictions, and ideal usage related to imaging methods and other symptomatic modalities [5]. Through a top to bottom examination of these biochemical markers, this paper plans to highlight their importance in early disease identification and forecast, consequently adding to the more extensive talk on improving malignant growth conclusion and patient results.

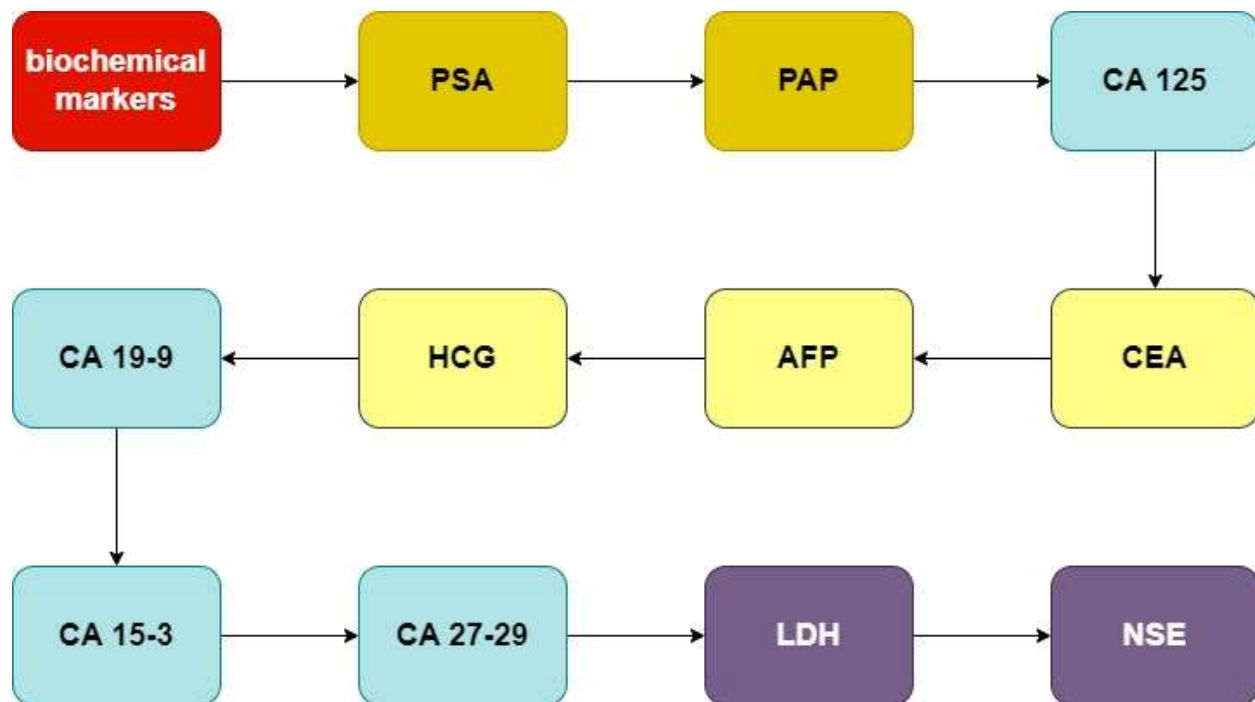


Fig 1 significance of various biochemical markers in cancer pathology

Prostate-Specific Antigen (PSA) and Prostatic Acid Phosphatase (PAP)

Prostate-specific antigen and PAP are basic markers in prostate malignant growth screening and checking. Raised degrees of prostate-specific antigen frequently show prostate irregularities, supporting early identification. Be that as it may, their explicitness and responsiveness stay under a magnifying glass, requiring extra tests for affirmation. Prostate-specific antigen and PAP are crucial biomarkers utilized overwhelmingly with regards to prostate disease [6]. Their jobs in early recognition, anticipation assurance, and checking treatment reaction have been instrumental in dealing with this common harm.

Prostate-specific antigen is a protein created by the prostate organ and is usually raised in prostate malignant growth. While it's a fundamental device for screening and observing, its particularity and responsiveness have been subjects of discussion [7]. Raised prostate-specific antigen levels can likewise emerge because of harmless prostatic circumstances, prompting misleading positive outcomes. Notwithstanding, prostate-specific antigen stays an important marker, particularly when utilized in blend with other symptomatic strategies. Late headways in

public service announcement testing, including the usage of public service announcement speed and thickness, have upgraded its explicitness for prostate malignant growth identification.

PAP is a protein created by the prostate organ, and its levels can likewise be raised in prostate disease. Notwithstanding, its job has reduced with the approach of public service announcement testing, as public service announcement has demonstrated to be more delicate and explicit [8]. PAP may be utilized in unambiguous situations where public service announcement levels are uncertain or to separate specific prostate disease subtypes.

In spite of their importance in prostate malignant growth discovery, both public service announcement and PAP have impediments. Misleading positive and bogus adverse outcomes can happen, affecting their dependability for individual patient finding [9]. Besides, their powerlessness to recognize forceful and slothful types of prostate disease represents a test in treatment navigation. The utilization of public service announcement and PAP related to DRE and imaging strategies, for example, X-ray has become standard practice. Furthermore, the developing scene of biomarker research plans to distinguish novel markers that can supplement or work on the particularity and responsiveness of public service announcement and PAP tests, working with more precise prostate disease discovery and forecast assurance [10]. Proceeded with research is imperative to improve the utility of public service announcement and PAP, tending to their limits and refining their application in the clinical setting. Incorporating these markers into extensive screening conventions stays significant for early identification and compelling administration of prostate malignant growth [11].

CA 125

CA 125, transcendently related with ovarian malignant growth, has shown guarantee in distinguishing beginning phase sickness, repeat observing, and surveying therapy reaction. Its job stretches out to other gynecological malignancies also. CA 125, a high sub-atomic weight glycoprotein, is a biomarker fundamentally connected with ovarian disease, in spite of the fact that it can likewise be raised in other gynecological malignancies and non-dangerous circumstances [12].

CA 125 has been a foundation in the administration of ovarian disease. Raised degrees of CA 125 in the blood can show ovarian malignant growth, especially in postmenopausal ladies. It

is especially helpful when observed over the long run, as a huge expansion in CA 125 levels might flag sickness movement or repeat. CA 125 guides in the conclusion of ovarian disease, particularly related to other demonstrative techniques like imaging (ultrasound, X-ray, CT filters) and actual assessment. Also, it adds to forecast assurance, corresponding more significant levels with further developed phases of the sickness and less fortunate results.

Regardless of its importance, CA 125 has constraints, as raised levels can likewise happen in non-malignant circumstances like endometriosis, period, and pelvic provocative illness. Consequently, it may not be explicit enough for solitary use in diagnosing ovarian malignant growth. CA 125 fills in as a significant marker for checking therapy reaction in ovarian malignant growth patients. A decrease in CA 125 levels after treatment commencement frequently demonstrates a positive reaction, while rising levels might propose illness movement or repeat, provoking further examination or change of treatment methodologies [13]. Continuous examination intends to work on the particularity and responsiveness of CA 125 as a biomarker for ovarian disease. This incorporates consolidating CA 125 with other biomarkers or imaging procedures to upgrade symptomatic exactness and better separate among harmless and threatening circumstances. CA 125 assumes an essential part in ovarian disease determination, guess, and treatment observing. While it's an important device, its utility should be viewed as related to other clinical data and demonstrative strategies to guarantee exact evaluation and the executives of ovarian malignant growth patients.

Carcinoembryonic Antigen (CEA)

CEA is a generally utilized biomarker for gastrointestinal tumors, particularly colorectal disease. It aids guess, treatment assessment, and repeat observation. Notwithstanding, its responsiveness may be restricted in specific settings [14]. CEA is a glycoprotein biomarker related with different tumors, most outstandingly colorectal disease, however it can likewise be raised in different malignancies and non-destructive circumstances.

CEA has been widely considered and used as a biomarker for colorectal disease. Raised degrees of CEA in the blood can show the presence of colorectal malignant growth and are frequently utilized for checking illness movement, evaluating treatment reaction, and recognizing repeat after a medical procedure [15]. While ordinarily connected with colorectal disease, CEA levels may likewise ascend in different malignancies, for example, pancreatic, bosom, lung, and

gastric tumors. Notwithstanding, its awareness and explicitness fluctuate among these different malignant growth types. CEA is helpful in diagnosing colorectal disease, particularly related to other demonstrative strategies like imaging and endoscopic assessments. Moreover, it fills in as a prognostic pointer, with more elevated levels frequently connected with cutting edge phases of the illness and a less fortunate guess.

One of the constraints of CEA is its absence of particularity, as levels can likewise be raised in non-harmful circumstances like aggravation, smoking, and certain gastrointestinal problems. Consequently, CEA alone isn't adequate for diagnosing malignant growth however is a significant instrument when joined with other clinical data and tests. CEA levels are often observed during and after malignant growth treatment. A decrease in CEA levels after a medical procedure or treatment frequently shows a positive reaction to therapy, while tireless or rising levels might propose repeat or protection from therapy [16]. Continuous examination expects to upgrade the utility of CEA as a biomarker, incorporating investigating its part in mix with other biomarkers or imaging procedures to work on demonstrative precision and recognize harmless and dangerous circumstances all the more successfully. In synopsis, while CEA is a significant biomarker, its explicitness impediments require wary translation. At the point when utilized related to other symptomatic apparatuses, CEA contributes altogether to the analysis, forecast, and checking of different tumors, especially colorectal malignant growth.

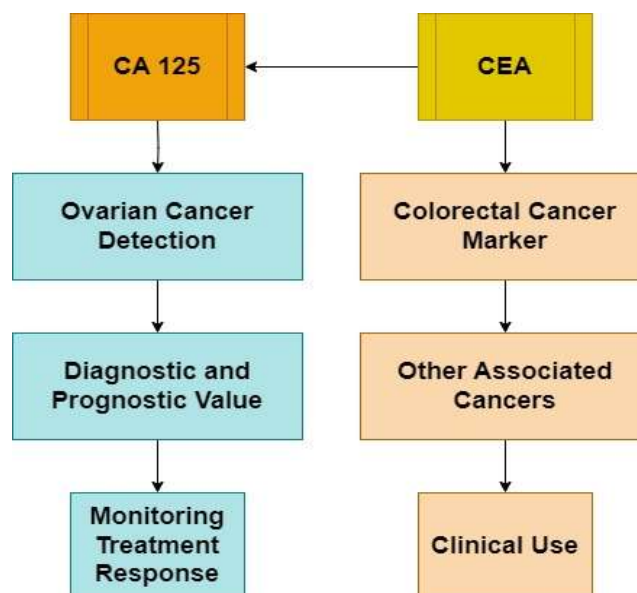


Fig 2 classification of CA 125 & CEA

Alpha-Fetoprotein (AFP) and Human Chorionic Gonadotropin (HCG)

AFP and HCG are fundamental in diagnosing and checking microbe cell growths and certain liver tumors. They help in distinctive cancer types, directing therapy choices, and surveying restorative reactions [17]. AFP and HCG are significant biomarkers basically connected with explicit sorts of disease, supporting conclusion, guess, and treatment observing.

AFP is prominently raised in liver diseases, especially HCC. It is utilized as a biomarker in screening, diagnosing, and observing HCC, particularly in high-risk populaces, for example, those with persistent liver sicknesses or cirrhosis [18]. Raised AFP levels are likewise seen in specific microbe cell growths, including testicular disease and ovarian microorganism cell cancers. It fills in as a marker for diagnosing and checking treatment reaction in these malignancies.

Microorganism Cell Growths and Trophoblastic Sicknesses: HCG is transcendently related with microbe cell growths, especially testicular disease, and trophoblastic infections like choriocarcinoma and gestational trophoblastic sickness. Raised HCG levels help in determination and observing treatment reaction in these circumstances.

In uncommon cases, raised HCG levels can likewise happen in different malignant growths, including lung and gastrointestinal diseases. Both AFP and HCG assume basic parts in diagnosing explicit diseases and checking therapy reactions, particularly with regards to microbe cell growths and specific sorts of liver tumors [19]. Notwithstanding, their rise in non-carcinogenic circumstances or different malignancies requires cautious translation and frequently requires extra tests for affirmation. These biomarkers are basic in clinical work on, directing treatment choices and surveying illness movement. Consolidating their estimations with imaging methods helps in precise finding and observing of malignant growth patients. Continuous exploration means to refine their utility and investigate their likely in mix with other biomarkers or imaging modalities to work on demonstrative exactness and therapy adequacy for these particular tumors [20].

CA 19-9, CA 15-3, and CA 27-29

These markers have utility in different malignancies, including pancreatic, bosom, and gastrointestinal tumors [21]. CA 19-9, for example, aids pancreatic disease determination, guess, and treatment observing. CA 19-9, CA 15-3, and CA 27-29 are biomarkers related with different sorts of malignant growth, supporting conclusion, anticipation, and treatment observing. CA 19-9

is normally utilized as a biomarker for pancreatic disease. Raised degrees of CA 19-9 in the blood are seen in numerous pancreatic disease cases. It supports analysis, particularly when joined with imaging studies, and is significant in observing treatment reaction and identifying repeat after treatment.

CA 15-3 is related with bosom malignant growth. Raised CA 15-3 levels can show the presence of bosom disease, despite the fact that it isn't suggested for essential screening. It is much of the time utilized in observing sickness movement, particularly in cutting edge bosom malignant growth cases, and to survey therapy reaction and repeat.

CA 27-29 is additionally connected to bosom malignant growth and is especially utilized in observing the course of the sickness, assessing therapy reaction, and identifying repeat in bosom disease patients. Like CA 15-3, it isn't utilized as an essential evaluating instrument for bosom disease [22]. These markers assume fundamental parts in the administration of explicit diseases, helping with finding, visualization, and treatment checking. Be that as it may, they are not disease explicit and might be raised in harmless circumstances or different malignancies, requiring alert in their understanding. At the point when utilized related to imaging strategies and other clinical data, they contribute fundamentally to the far reaching appraisal of malignant growth patients. Proceeded with research plans to refine the utility of these biomarkers, work on their explicitness and responsiveness, and investigate their possible in mix with different markers or imaging modalities to improve symptomatic exactness and therapy viability in different malignant growths.

Lactate Dehydrogenase (LDH) and Neuron-Specific Enolase (NSE)

LDH and NSE act as markers in different diseases, like neuroendocrine growths and hematological malignancies. They help in forecast assurance, illness observing, and treatment assessment [23].

LDH and NSE are biomarkers used in diagnosing, guessing, and observing different diseases, especially in neuroendocrine growths and hematological malignancies. LDH is a catalyst present in cells all through the body, and its height in the blood might demonstrate cell harm or sickness. While not well defined for any malignant growth type, LDH levels are much of the time raised in tumors, including lymphoma, leukemia, and melanoma [24]. In certain malignant growths, particularly lymphoma and metastatic melanoma, higher LDH levels at analysis are

related with more forceful sickness and less fortunate guess. LDH levels can act as a prognostic marker, helping with risk delineation and treatment arranging.

NSE is a catalyst principally connected with neuroendocrine growths, including neuroblastoma, little cell cellular breakdown in the lungs, and neuroendocrine cancers of different starting points. Raised NSE levels are demonstrative of neuroendocrine separation in growths. NSE levels are utilized as prognostic markers in neuroendocrine growths [25]. Tirelessly undeniable levels during treatment or after careful evacuation of the cancer might show lingering infection or repeat. Checking NSE levels helps in evaluating treatment reaction and sickness movement. Both LDH and NSE are critical in oncology as markers that give knowledge into the sickness' forcefulness, anticipation, and therapy reaction, particularly in unambiguous disease types. Notwithstanding, their rise can likewise happen in non-malignant circumstances, requiring cautious translation and relationship with clinical discoveries and other demonstrative tests. Research keeps on investigating the job of LDH and NSE in various tumors and expects to refine their utility, further develop particularity, and distinguish their ideal use in directing treatment choices and observing sickness movement in different malignancies.

Results and discussion:

Notwithstanding their utility, challenges continue with respect to the particularity, responsiveness, and normalization of these markers. Progressing research centers around recognizing novel biomarkers and working on existing tests to improve their demonstrative and prognostic precision [26]. The utilization of biochemical markers in malignant growth determination and the board has altogether progressed our comprehension and way to deal with this mind boggling sickness. Nonetheless, a few difficulties persevere, and continuous examination expects to address these while investigating future headings to improve the utility of biomarkers in oncology.

Numerous biomarkers miss the mark on essential explicitness and responsiveness for exact disease discovery and separation from harmless circumstances or different malignancies. Further developing these perspectives stays a huge test. Normalization of examines and techniques for estimating biomarkers is essential for guaranteeing consistency and exactness across labs. Endeavors to approve and lay out normalized conventions are continuous. Most biomarkers are not malignant growth explicit and can be raised in different illnesses or physiological

circumstances, prompting bogus up-sides or negatives. Consolidating numerous markers or incorporating them with imaging methods might upgrade precision.

Biomarkers with the potential for early location of malignant growth or anticipating infection movement and treatment reaction are exceptionally pursued. Research centers around distinguishing novel markers that can satisfy these jobs actually [27]. Headways in innovation, including sub-atomic science procedures, man-made brainpower, and nanotechnology, offer chances to foster more delicate, explicit, and fast biomarker discovery techniques.

Fitting treatment methodologies in light of a patient's biomarker profile and hereditary cosmetics is a promising methodology in customized medication. Biomarkers assume an essential part in directing designated treatments. Investigating new biomarkers, like flowing growth DNA (ctDNA), microRNAs, and metabolomics, and coordinating multi-omics approaches offer an exhaustive comprehension of disease science and possible new roads for finding and treatment. Coordinating biomarkers into routine clinical practice requires tending to cost-adequacy, openness, and guaranteeing that their utilization altogether influences patient results. Later on, refining existing biomarkers, finding novel ones, and coordinating them into far reaching analytic and prognostic calculations will probably alter disease determination, treatment, and observing. Cooperation between analysts, clinicians, and innovation specialists stays crucial in conquering current difficulties and saddling the maximum capacity of biomarkers in oncology.

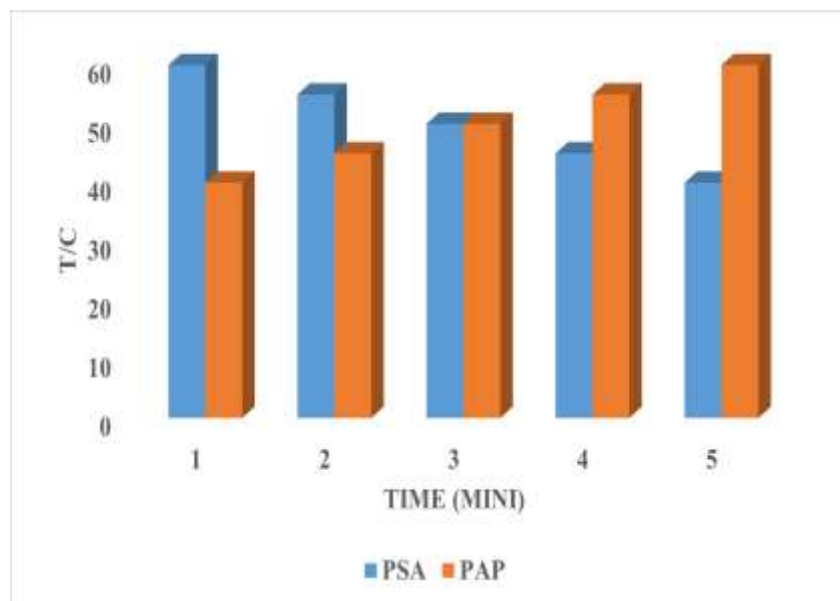


Fig 3 T/C variations of PSA &PAP

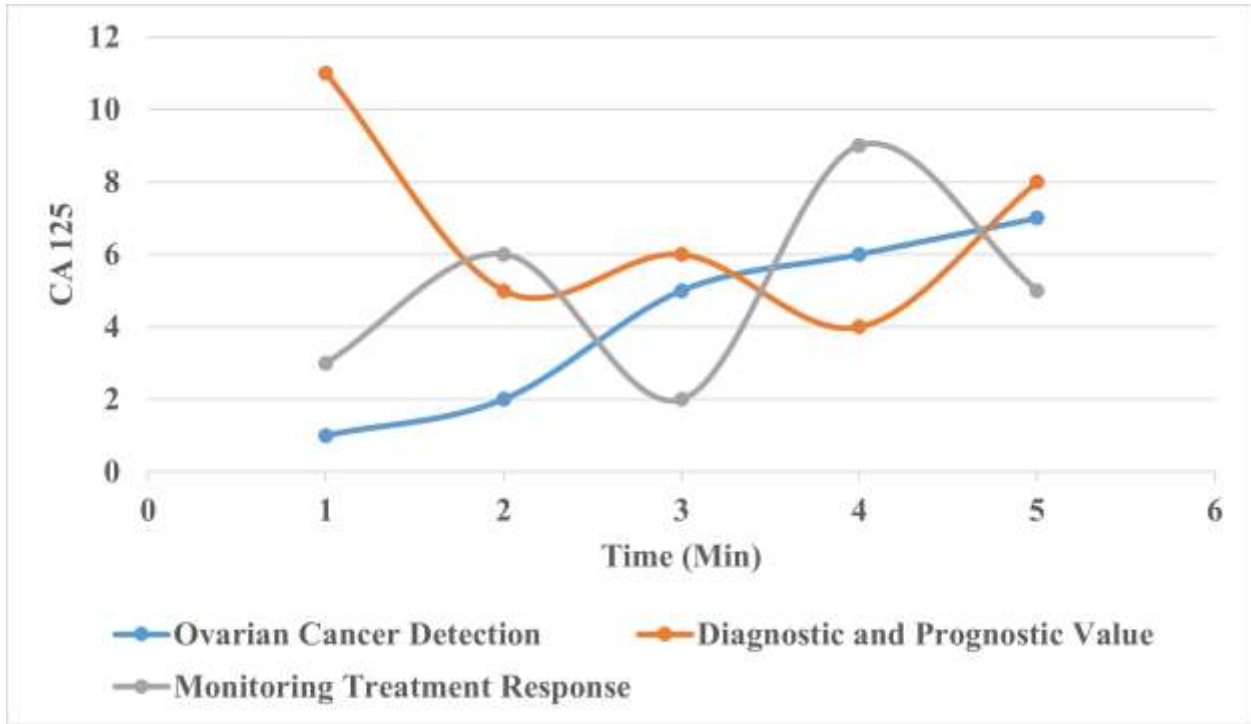


Fig 4 Sources of CA 125

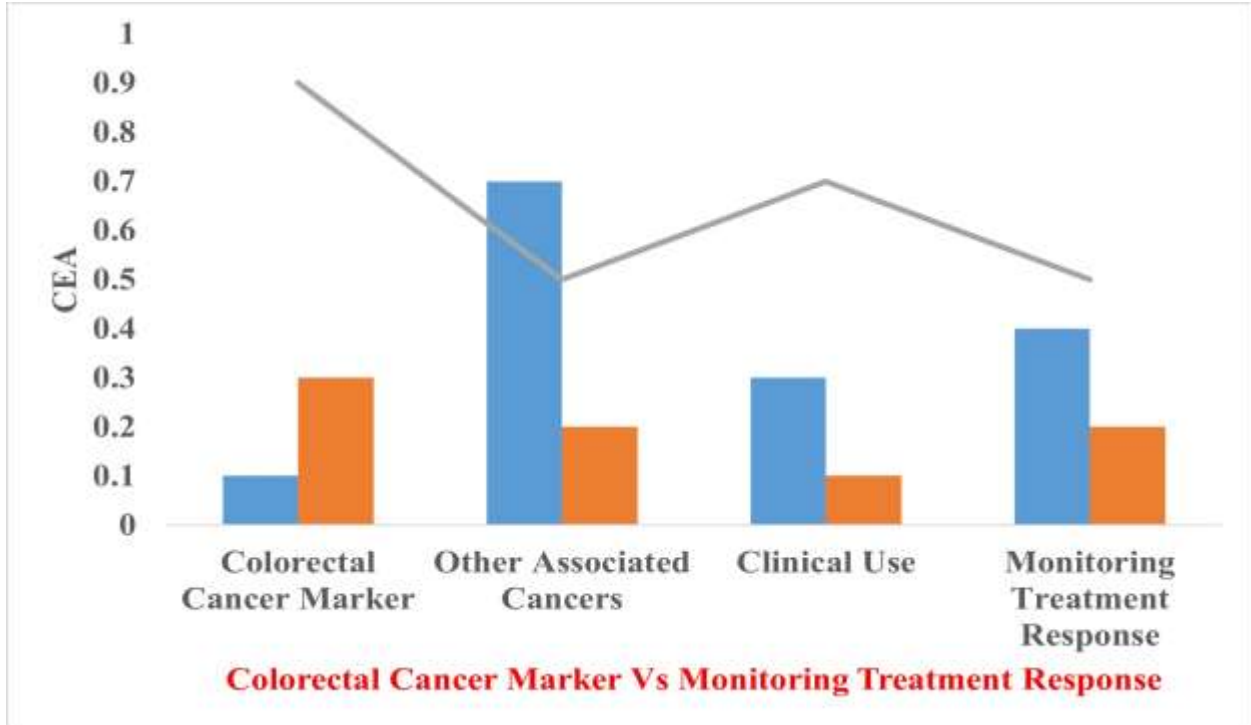


Fig 5 CCM Vs MTR

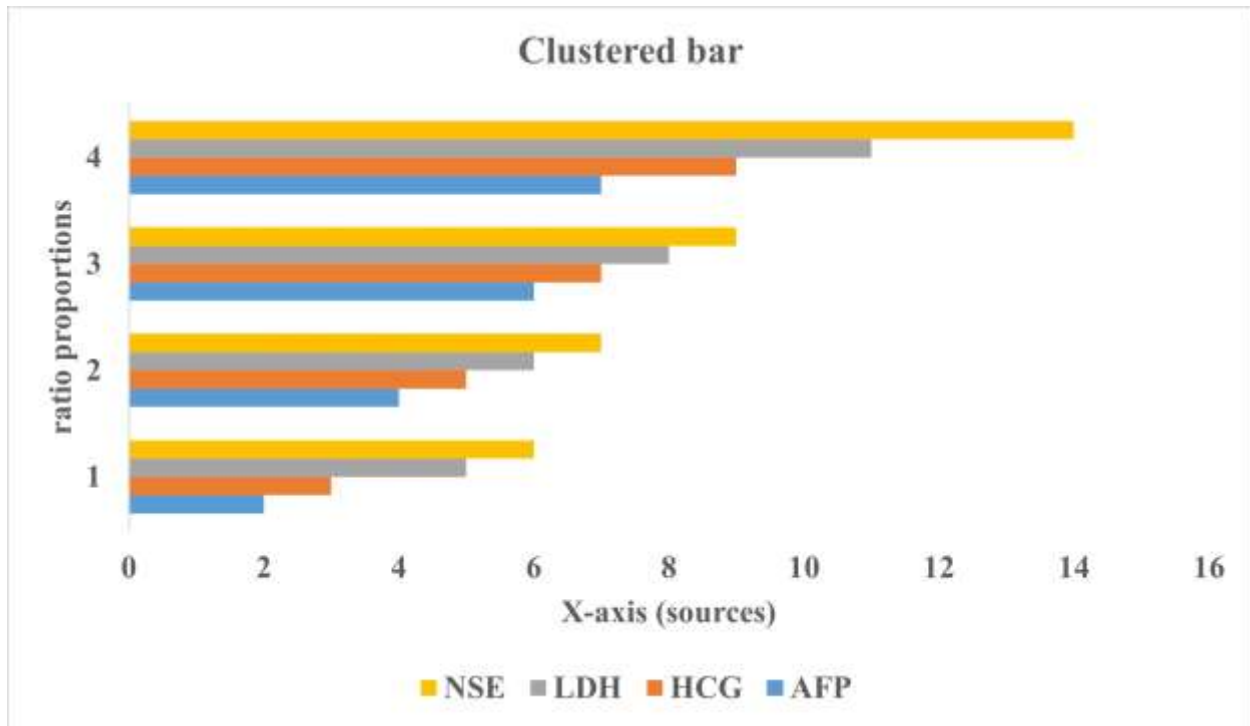


Fig 6 Clustered bar for ratio proportions

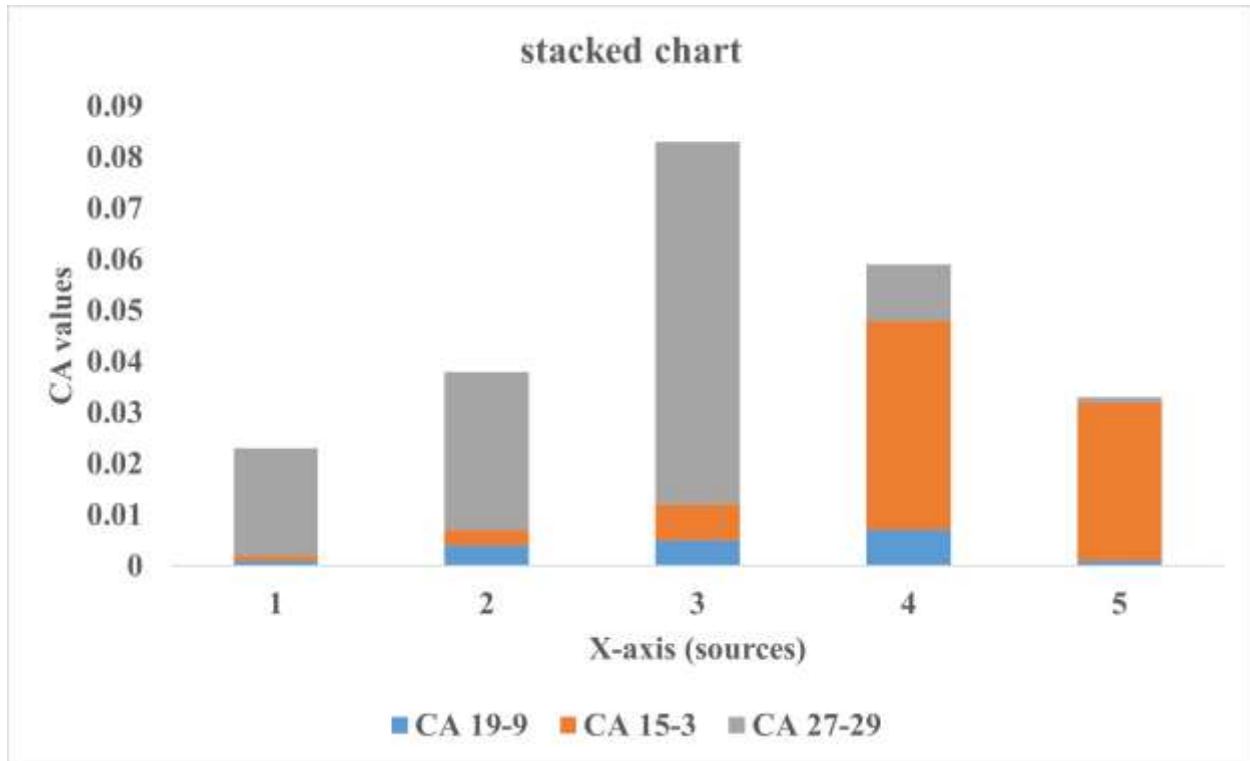


Fig 7 Sources of CA values

Conclusion

The biochemical markers assume an essential part in the scene of malignant growth conclusion, guess, and treatment observing. Notwithstanding their importance in supporting early discovery and directing remedial choices, a few difficulties continue, going from limits in explicitness and aversion to normalization and approval issues. Markers like public service announcement, CA 125, CEA, AFP, HCG, LDH, NSE, and others have altogether added to malignant growth the executives. Notwithstanding, their utility frequently requires careful understanding related to clinical setting and other demonstrative modalities. Future headings in biomarker research expect to address these difficulties by investigating novel markers, utilizing trend setting innovations for additional exact estimations, and coordinating multi-omics ways to deal with improve analytic precision and prognostic worth. The quest for customized medication, wherein treatment methodologies are custom-made in view of individual biomarker profiles, holds extraordinary commitment for working on understanding results.

Cooperation between scientists, clinicians, and innovation specialists stays basic in saddling the maximum capacity of biomarkers. As examination advances, refining existing markers and finding new ones will probably reform malignant growth care, introducing a time of more exact conclusion, better forecast, and custom-made treatment methodologies. Biomarkers, as a feature of a thorough methodology, will keep on being instrumental in the battle against disease, at last working on tolerant results and personal satisfaction.

Funding: Nil.

DATA AVAILABILITY:

All datasets generated or analyzed during this study are included in the manuscript.

Institutional Ethical Committee Approval

The paper is a review article so no ethical approval is required.

Informed Consent

Not applicable.

Use of Artificial Intelligence:

The author has taken the assistance of Grammarly and Google gemini for better readability and language improvement, but have rechecked the contents for their authenticity and take the full responsibility.

Authors' contributions:

All author equally contributed for concept, data collection, writing manuscript, review and publication

References

1. L. Mansi, V. Cuccurullo, and R. Grassi, "Diagnostic imaging and pathology," in *Advanced Imaging Techniques in Clinical Pathology*, pp. 107–111, Springer, Berlin, Germany, 2016.
2. M. Aiello, C. Cavaliere, D. Fiorenza et al., "Neuroinflammation in neurodegenerative diseases: current multi-modal imaging studies and future opportunities for hybrid PET/MRI," *Neuroscience*, vol. 403, pp. 125–135, 2019.
3. A. Surov, H. J. Meyer, and A. Wienke, "Associations between apparent diffusion coefficient (ADC) and KI 67 in different tumors: a meta-analysis. Part 2: ADCmin," *Oncotarget*, vol. 9, no. 9, pp. 8675–8680, 2018.
4. F. A. G. d. R. Araujo and U. Oliveira Jr, "Current guidelines for prostate cancer screening: a systematic review and minimal core proposal," *Revista da Associação Médica Brasileira*, vol. 64, no. 3, pp. 290–296, 2018.
5. A. Surov, H. J. Meyer, A.-K. Höhn, K. Winter, O. Sabri, and S. Purz, "Associations between [18F]FDG-PET and complex histopathological parameters including tumor cell count and expression of KI 67, EGFR, VEGF, HIF-1 α , and p53 in head and neck squamous cell carcinoma," *Molecular Imaging and Biology*, vol. 21, no. 2, pp. 368–374, 2019.
6. M. Scimeca, C. Antonacci, N. Toschi et al., "Breast osteoblast-like cells: a reliable early marker for bone metastases from breast cancer," *Clinical Breast Cancer*, vol. 18, no. 4, pp. e659–e669, 2017.
7. M. Bonanno, N. Urbano, R. Bonfiglio, O. Schillaci, and E. Bonanno, "Breast osteoblast-like cells: a new biomarker for the management of breast cancer," *British Journal of Cancer*, vol. 119, no. 9, pp. 1129–1132, 2018.

8. M. Yousefi, S. Dehghani, R. Nosrati, M. Ghanei, A. Salmaninejad, and S. Rajaie, “Current insights into the metastasis of epithelial ovarian cancer-hopes and hurdles,” *Cellular Oncology*, vol. 43, no. 4, pp. 515–538, 2020.
9. C. E. Staicu, D. V. Predescu, C. M. Rusu et al., “Role of microRNAs as clinical cancer biomarkers for ovarian cancer: a short overview,” *Cells*, vol. 9, no. 1, 2020.
10. U.S. National Library of Medicine, 2020, <https://clinicaltrials.gov/ct2/results?term=microrna&cond=Ovarian+Cancer>.
11. H. Shi, H. Shen, J. Xu, S. Zhao, S. Yao, and N. Jiang, “MiR-143-3p suppresses the progression of ovarian cancer,” *American Journal of Translational Research*, vol. 10, no. 3, pp. 866–874, 2018.
12. M. Zhang, B. B. Dong, M. Lu et al., “miR-429 functions as a tumor suppressor by targeting FSCN1 in gastric cancer cells,” *OncoTargets and Therapy*, vol. 9, pp. 1123–1133, 2016.
13. Y.-W. Chung, H.-S. Bae, J.-Y. Song et al., “Detection of microRNA as novel biomarkers of epithelial ovarian cancer from the serum of ovarian cancer patient,” *International Journal of Gynecological Cancer*, vol. 23, no. 4, pp. 673–679, 2013.
14. H. Zheng, L. Zhang, Y. Zhao et al., “Plasma miRNAs as diagnostic and prognostic biomarkers for ovarian cancer,” *PLoS One*, vol. 8, no. 11, Article ID e77853, 2013.
15. Xie W, Reder NP, Koyuncu CF, et al. Prostate cancer risk stratification via nondestructive 3D pathology with deep learning-assisted gland analysis. *Cancer Res* 2022; 82: 334–345.
16. Hanahan D. Hallmarks of cancer: new dimensions. *Cancer Discov* 2022; 12: 31–46.
17. Boehm KM, Khosravi P, Vanguri R, et al. Harnessing multimodal data integration to advance precision oncology. *Nat Rev Cancer* 2022; 22: 114–126.
18. Sammut SJ, Crispin-Ortuzar M, Chin SF, et al. Multi-omic machine learning predictor of breast cancer therapy response. *Nature* 2022; 601: 623–629.
19. Patsouris A, Diop K, Tredan O, et al. Rucaparib in patients presenting a metastatic breast cancer with homologous recombination deficiency, without germline BRCA1/2 mutation. *Eur J Cancer* 2021; 159: 283–295.
20. Liu L, Yu L, Li Z, et al. Patient-derived organoid (PDO) platforms to facilitate clinical decision making. *J Transl Med* 2021; 19: 40.
21. Voabil P, de Bruijn M, Roelofsen LM, et al. An ex vivo tumor fragment platform to dissect response to PD-1 blockade in cancer. *Nat Med* 2021; 27: 1250–1261.

22. van Wijk LM, Kramer CJH, Vermeulen S, et al. The RAD51-FFPE test; calibration of a functional homologous recombination deficiency test on diagnostic endometrial and ovarian tumor blocks. *Cancers (Basel)* 2021; 13: 2994.
23. Llop-Guevara A, Loibl S, Villacampa G, et al. Association of RAD51 with homologous recombination deficiency (HRD) and clinical outcomes in untreated triple-negative breast cancer (TNBC): analysis of the GeparSixto randomized clinical trial. *Ann Oncol* 2021; 32: 1590–1596.
24. Eikesdal HP, Yndestad S, Elzawahry A, et al. Olaparib monotherapy as primary treatment in unselected triple negative breast cancer. *Ann Oncol* 2021; 32: 240–249.
25. Irmisch A, Bonilla X, Chevrier S, et al. The Tumor Profiler Study: integrated, multi-omic, functional tumor profiling for clinical decision support. *Cancer Cell* 2021; 39: 288–293.
26. Xing, Z.; Luo, Z.; Yang, H.; Huang, Z.; Liang, X. Screening and identification of key biomarkers in adrenocortical carcinoma based on bioinformatics analysis. *Oncol. Lett.* 2019, 18, 4667–4676.
27. Rege, J.; Turcu, A.F.; Else, T.; Auchus, R.J.; Rainey, W.E. Steroid biomarkers in human adrenal disease. *J. Steroid Biochem. Mol. Biol.* 2019, 190, 273–280.