Biological biomarkers of cancer prognosis

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Introduction

- Antibody-based detection methods have allowed the evaluation of many biological compounds of clinical importance in cancer prognosis.
- These include proteins in bodily fluids, proteins in tumor tissue or lymph nodes, and cell types identifiable by protein expression.
- There is an ongoing effort to discover additional molecular biological biomarkers for their significance in predicting survival and providing potential targets for research.
- Knowing the likely course of disease can inform the goals of care, such as implementing advanced directives or switching from a curative to palliative approach.
- Accurate estimates of prognosis are required to ensure that patients are maximizing quality of life (QOL) while minimizing adverse events towards the end of life.

Objective

- To systematically summarize the literature on molecular biomarkers associated with cancer outcome.

Methods

- A literature search was conducted on Medline and Embase utilizing keywords such as "cancer," "inflammation," "prognosis," "inflammation" and "biomarkers."
- Articles that reported on uncommon biological biomarkers of prognosis were selected for inclusion.
- Information regarding the cancer type, interventions received, and the impact on prognosis and significance was extracted.
- Outcomes measured include: Overall survival (OS), Cancer specific survival (CSS), Disease-free survival (DFS) and Recurrence-free survival (RFS)

Results

- A total of 28 studies comprising of 5,234 patients found associations between 45 uncommon molecular biomarkers and prognosis in more than 15 types of primary malignancies.

Protein-based biomarkers in bodily fluids

- 13 studies, of which 8 performed multivariate analysis, showin g12 significant proteins
- 4 biomarkers: hemoglobin (Hb), carcinoembryonic antigen (CEA), pentraxin 3 (PTX3), and interleukin 6 (IL6), were found to be significantly associated with poor CSS, DFS, or OS, in multiple univariate analyses, and were also found to be significant in multivariate analysis in at least one study
- Additional biomarkers that are independent predictors of survival include the interleukins IL1, IL10 and IL8, vascular endothelial growth factor (VEGF), and prostate-specific antigen (PSA)
- In multivariate, elevated blood CEA was associated with the greatest risk of death (Odds Ratio (OR) 12.5, p<0.001), and elevated blood IL1 was associated with the greatest risk of recurrence (Hazard Ration (HR) 11.84, p=0.01)

Protein-based biomarkers found in tissues

- 12 studies assessed for molecular biomarkers detected through immunohistochemistry of tissues, and 6 studies with multivariable analysis found 5 proteins independently associated with OS, DFS, or CSS
- High PTX3, FGF, AHNAK, STAT3 associated with poor DFS, OS or CSS
- High IL6R associated with improved CSS
- PTX3 had highest HR for OS (HR 8.53)

Cell-based biomarkers found in tissues

- 7 studies, all with multivariable analysis, identified 8 cell types of which 3 were independent significant predictors of outcome
- Combination of KRS(+) tumour cells and KRS(-) TAI cells associated with shorter OS (HR 2.22, p=0.001)
- MRP14(+) inflammatory cells associated with longer OS (RR 0.643, p=0.046)

Discussion

- ❖ Our review has summarized 45 unique molecular biomarkers are associated with cancer outcome. These are often part of recurring physiological pathways that become dysregulated in cancers.
- ❖ Proteins involved in the inflammatory response have frequently been identified as biomarkers predictive of adverse outcomes.
- ❖ This includes pro-inflammatory signaling molecules such as IL1, IL6, IL8, and PTX3, but also the anti-inflammatory IL10 (3, 4, 14, 20). Of particular significance is PTX3, a pro-inflammatory protein involved with the innate immune response and tissue remodeling that belongs to the same molecular class as the better known C-reactive protein (CRP).

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Conclusion

- ❖ Many molecular biomarkers found to be associated with prognosis are part of the overlapping pathways of inflammation and oxidative stress.
- ❖ Identification of prognostic biomarkers has the potential to highlight aspects of physiology that lead to poor prognosis and assist in the identification of therapeutic targets.
- ❖ Ultimately, understanding the nature of biological biomarkers not only improves prognosis, but also facilitates the identification of potential interventional targets for personalized therapy