A review of biomarkers relating to cancer-related symptom burden and quality of life

Leigha Rowbottom[1], MD(C), Stephanie Chan[1], BSc(C), Bo Angela Wan[1], MD(C), Pearl Zaki[1], BSc(C), Matthew Choi[1], BSc, Anthony Furfari[1], MD(C), Rachel McDonald[1], MD(C), Carlo DeAngelis[1], PharmD, Azar Azad[2,3,4], PhD, Ronald Chow[1], BMSc(C), Henry Lam[1], MLS, Edward Chow[1], MBBS and George S Charames[3,4,5,], PhD*

Radiation Oncology UNIVERSITY OF TORONTO

[1]Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto
[2]Mount Sinai Services Inc., Toronto
[3]Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto
[4]Laboratory Medicine and Pathobiology, University of Toronto, Toronto
[5]Lunenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto

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Introduction

- Cancer and associated treatments often have significant impact on patients and can manifest in a variety of symptoms leading to negative outcomes on health-related quality of life (HRQOL).
- Certain symptoms may occur in conjunction, also referred to as a symptom cluster, which can lead to aggregate burden on the patient.
- Symptom clusters may occur together as there may be one true underlying etiology, which if identified could provide therapeutic targets for enhanced symptom management.
- Biomarkers may provide clues to physicians as to what the cause of a symptom or symptom cluster is, as well as to help identify symptoms in non-communicative patients.

Objective

To summarize the available literature regarding biological and genetic biomarkers related to cancer-related symptoms and quality of life (QOL) in cancer patients.

Methods

A systematic literature review was conducted using Medline and Embase (1947 to 2016 Week 16). A combination of keywords was utilized including “inflammation”, “cancer pain”, “neoplasm”, “biological marker”, “allele”, and “genomics”. Articles were limited to studies conducted in humans and reported in English. The literature search resulted in a total of 5,480 articles that were screened by title then abstract.

Results

A total of 41 articles were identified for inclusion

Fatigue

- Increased levels of pro-inflammatory serum cytokines and their receptors were associated with fatigue in patients undergoing radiotherapy.
- Multiple studies found elevated CRP being correlated with fatigue
- Several studies showed that patients experiencing severe fatigue were found to have elevated levels of lymphocytes such as T-lymphocytes, neutrophils, and monocytes
- No genetic variations were identified

Cancer Cachexia

- Cachectic patients across 7 cancer types were all found to have elevated IL-6, IL-8 and absolute neutrophil levels. Cachectic and Pre-cachectic were also found to have elevated angiotensin II, TGFB1, and also increased mRNA expression of neutrophil-derived proteases
- Other studies showed that cachectic patients also head increased ubiqutin mRNA, with decreased overall testosterone levels
- Similar to other markers of QoL, elevated levels of pro-inflammatory cytokines (CRP, TNF-R1, and TNF-a) is associated with poorer outcomes such as cachexia.

Depression, Anxiety, and Neurocognitive Complaints

- Val66Met variant of BNDF, increased CRP were found to be significant predictors of depressive symptoms in early-stage breast cancer patients
- Another study showed that increased IL-10, and decreased IL-4 were heavily associated with increased anxiety
- Memory performance was also found to be related to soluble levels of TNF-RII

Symptom Burden and Quality of Life

- IL6 was found to be correlated with pain and reduced QoL in breast cancer survivors
- Others reported that IL6 was linked to disturbed sleep, distress, and mood interference patients suffering from colorectal cancer and various other cancers
- CRP levels were evaluated in 3 different studies, with each reported that elevated CRP being linked to poorer HRQoL.
- Additional studies showed that higher baseline levels of CRP, VEGF, and neutrophil:lymphocyte ratio was associated with anorexia, fatigue and poorer QoL
- Variations of IL1B, JAK2, IL1R2, NFKB2, TNFR1 were all found to have provided differential experiences in QOL from cancer patients
- 174GG genotype for the IL6 gene in non-Hispanic white patients was found to be a

Discussion

- Appropriate evaluation of patient risk for pain, fatigue, nausea, and depression, not only helps with outcomes but also the guidance provided by healthcare providers to family members for appropriate care
- High levels of inflammatory protein biomarkers have been linked to increases in immunological biomarkers and poor cancer symptoms.
- Animal models studying the “cytokine-immunologic model” for cancer symptoms have shown that administrating pro-inflammatory agents generates sickness that mirrors cancer symptoms, and could be a potential treatment target
- Genetic analysis for genetic variants have produced mixed results but have potential

Selected references

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Conclusion

- this study highlights a complicated network of neuroendocrine-immuno-chemical-cognitive network that seems to modulate both cognitive and physical symptoms in cancer patients.
- Future research should look to delineate this relationship to better understand how these different systems integrate and connect with one another.

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