LONG-TERM FOLLOW-UP AFTER CANCER IN CHILDHOOD OR ADOLESCENCE: WHAT, HOW AND WHY?

BY:

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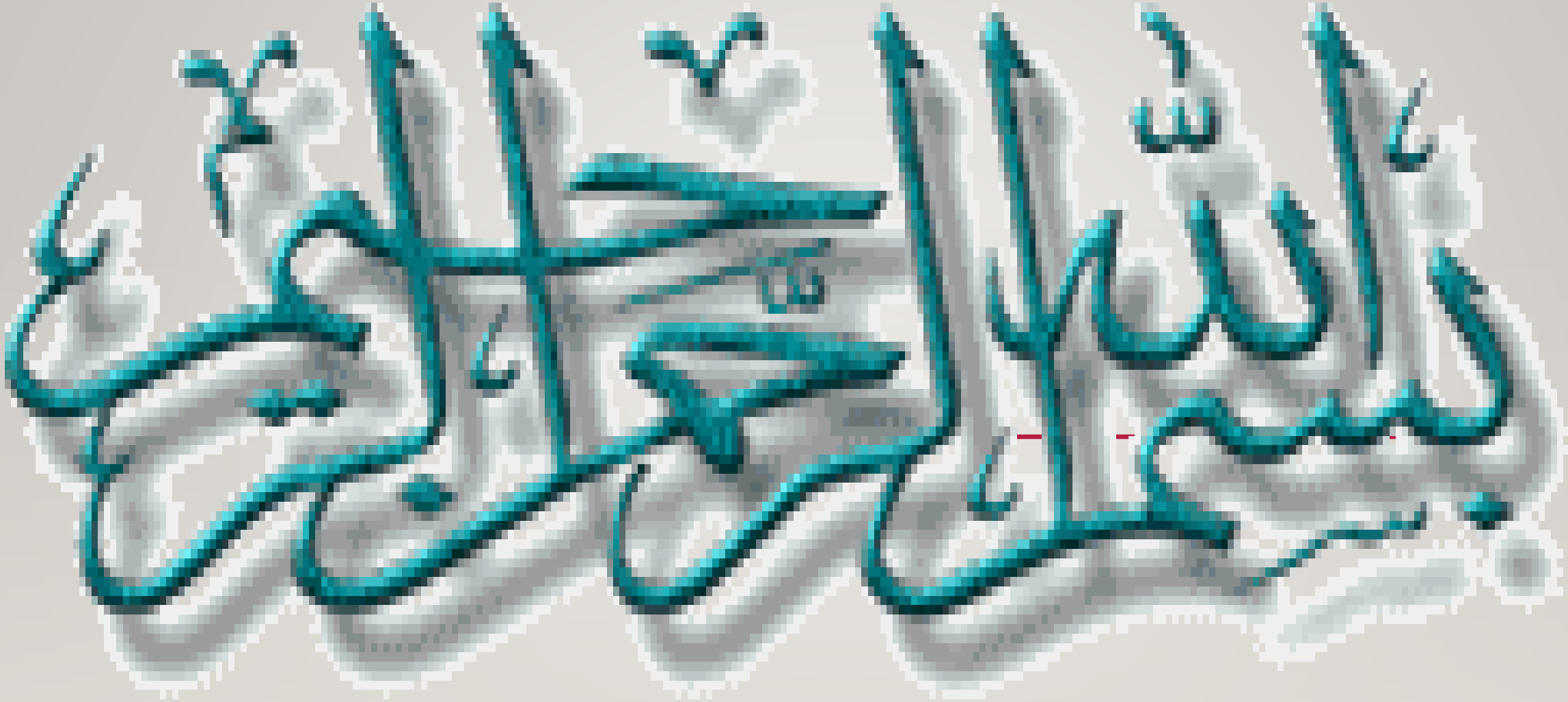

INTRODUCTION:

- Over the past several decades, significant improvements have been observed in the survival rates of children and adolescents diagnosed with cancer. In Europe, the five-year survival rate for children aged 0–14 years increased from 44% for those diagnosed in the 1970s to 64% in the 1980s, 74% in the 1990s, and 79% in the 2000s. Among adolescents aged 15–19 years, the survival rate rose from 50% in the 1970s to 63% in the 1980s, and 74% in the 1990s.

AIM OF STUDY ON LATE COMPLICATIONS:

- Research into late effects aims to support the development of standardized protocols that ultimately seek to optimize survival outcomes while minimizing the adverse effects associated with cancer treatment.

INTRODUCTION

- While these therapies are essential for improving survival, they are also associated with both acute and long-term adverse effects. Late effects refer to health complications that arise months or even years after the completion of cancer treatment, and may result from either the treatment itself or the underlying disease.
- Definitions of late effects vary, particularly in terms of the time interval post-treatment that qualifies as "late”. The impact of these effects on childhood and adolescent cancer survivors (CACS) is substantial.

INTRODUCTION

- Approximately 30% develop serious or life-threatening health problems, with some studies reporting this figure to rise to 40% three decades after diagnosis.
- Late effects often take years to manifest, and their incidence continues to rise over time, showing no clear plateau. This underscores the critical importance of long-term follow-up care and targeted interventions to mitigate the ongoing burden faced by survivors.

TYPE OF LATE EFFECTS:

- These effects, which include physical, psychological, and cognitive issues, affect over 60% of survivors and often persist or worsen with age. Common late effects involve the cardiovascular, endocrine, and musculoskeletal systems, as well as neurocognitive impairment, infertility, and the risk of subsequent malignancies.

VARIABLES OF LATE EFFECTS

- The characteristics of the primary disease,
- the type and intensity of treatment received,
- and individual patient factors.

SEX:

- Geenen et al. (2007) reported a relative risk (RR) for women
of 1.10 (95% CI: 1.03–1.18),
indicating that female survivors are at a significantly higher risk of developing late effects of at least moderate severity compared to male survivors.

AGE:

- By the age of 50, survivors had experienced an average of 17.1 chronic health conditions (CHCs) of any severity, including 4.7 grade 3–5 CHCs.

In contrast, the control group had an average of 9.2 CHCs across all grades, and 2.3 grade 3–5 CHCs.

This indicates that by age 50, survivors bear double the disease , with an excess of almost eight additional chronic conditions per person, two of which are disabling!

TYPE OF DISEASE, AND OTHER RISK FACTORS:

- The burden of CHCs is highest among survivors of central nervous system (CNS) tumor, and lowest among survivors of germ cell tumors.

When the type of cancer is not taken into account, Bhakta et al. (2017) identified three key risk factors associated with an increased burden of CHCs:

1. exposure to high doses of radiation to the brain or chest,
2. the era in which the patient was treated,
3. and older age at diagnosis.

CARDIOVASCULAR EFFECTS:

- The cardiovascular system is particularly vulnerable to two components of cancer treatment: cumulative anthracycline dose and cardiac radiation exposure.
- Patients receiving cumulative anthracycline doses below 205 mg/m² exhibit a 3.4-fold increased risk of developing heart failure (HF) compared to those not exposed to anthracyclines .
- This risk escalates to 11.4-fold at doses between 250–360 mg/m²,
- and further to 15-fold at doses exceeding 360 mg/m².

CARDIOVASCULAR EFFECTS:

- Similarly, higher doses of cardiac radiation increase the risk of HF and other cardiac diseases. Combined exposure to anthracyclines and cardiac radiation amplifies HF risk more than either treatment alone, even when less than 10% of the heart receives ≥30 Gy.
- The prevalence of cardiac conditions increases with age; incidence ranges from 4% to 24% in patients aged 30–39 years, rising to 10%–37% in those over 40 years.

ENDOCRINE COMPLICATIONS:

- The endocrine system is highly susceptible to damage from radiotherapy and gonadotoxic chemotherapy.
- Radiotherapy to various anatomical sites, including cranial, thoracic, neck, abdominal, pelvic, and genitourinary regions, can impair endocrine function due to the proximity of critical endocrine organs.
- CNS tumors, Hodgkin lymphoma, and leukemia are particularly associated with endocrine dysfunction.

ENDOCRINE DYSFUNCTION

- Brignardello et al. (2013) reported endocrine diseases in approximately 50% of CACS, with 48% of female and 63% of male survivors affected.

The most common conditions included:

- gonadal dysfunction,
- primary hypothyroidism,
- and growth hormone deficiency.

ENDOCRINE COMPLICATIONS: INFERTILITY

- Fertility impairment constitutes a significant subset of endocrine late effects. Gonadotoxic chemotherapy and radiotherapy not only disrupt hormone production but also reduce fertility potential in survivors. Approximately 30% of CACS experience infertility, although rates vary by treatment modality.
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INFERTILITY

- Fertility impairment constitutes a significant subset of endocrine late effects. Gonadotoxic chemotherapy and radiotherapy not only disrupt hormone production but also reduce fertility potential in survivors.
- Approximately 30% of CACS experience infertility, although rates vary by treatment modality. A German cohort study found infertility rates of 31% among female and 29% among male survivors, while other studies reported infertility in 15.9% of females and between 42% and 66% of males.

MUSCULOSKELETAL SYSTEM

1- Osteonecrosis presenting the highest relative risk .

2- Osteoporosis is the second most common late effect,

3- low bone mineral density, and osteoarthritis in up-to 30%

FATIGUE HEARING LOSS:

- Cancer-related fatigue (CRF), hearing loss affects between 19% and 42% of survivors depending on study parameters.
- Risk factors include:
- 1- female sex,
- 2- CNS tumor diagnosis,
- 3-presence of comorbid health conditions,
- 4- and endocrine disorders

HEARING LOSS PREVALENCE VARIES BY TUMOR TYPE, AND TREATMENT TYPE:

- 25% in CNS tumors,
- 23% in neuroblastomas,
- 21% in hepatic tumors,
- 16% in bone tumors and soft tissue sarcomas,
- and 20% in germ cell tumors.
- Treatments associated with increased hearing loss risk include platinum-based chemotherapy, cranial radiation, brain surgery, CSF shunting, and bone marrow transplantation.

NEUROCOGNITIVE IMPAIRMENT

- Radiation adversely affects overall neurocognitive function, but particularly processing speed, sustained attention, working memory, and executive function.
- With severity depending on radiation extent and total brain irradiation leading to the most profound impairments.
- Similarly, intrathecal chemotherapy's neurotoxic effects vary by dose, primarily impacting working memory, processing speed, and executive functioning.
- Additional contributors to neurocognitive deficits include hydrocephalus requiring shunting and brain surgery.

SUBSEQUENT MALIGNANT NEOPLASM

- Acute myeloid leukemia (16%), skin cancers (12%), central nervous system tumors (11%), thyroid cancer (12%) and bone tumors (5%).
- Up-to 30% of CACS exposed to thoracic radiotherapy develop breast cancer.
- The risk of thyroid cancer increases by 10 to 15 times,
- The risk of bone cancer rises linearly with radiation dose, reaching up to a 78-fold increase, when these regions are exposed.
- Radiation has a big impact on the development of brain tumors, so much so that the risk of a meningioma increases up to 568 times!

EFFECT OF CHEMOTHERAPY ON THE SECOND MALIGNANT NEOPLASM

- Etoposide and anthracyclines give an increased risk up to seven times to develop leukemia.
- Teepen et al. (2017) describes an impact of doxorubicin on the development of solid and breast tumors and an impact of cyclophosphamide on the occurrence of sarcomas in a dose-dependent fashion.
- Alkylating agents with a cumulative dose higher than 10 000mg/m^2 increases the risk on developing bone cancer 7-8 times.

PSYCHOLOGICAL LATE EFFECTS: (PTSD), ANXIETY, DEPRESSION, AND STRESS.

- A PTSD prevalence of 14.5%, with increased risk among survivors who received cranial radiation.
- Anxiety and depression risk are elevated in survivors with cardiovascular conditions.
- Female survivors, those reporting late effects, and survivors of CNS tumors are also more likely to experience higher stress levels.

CONCLUSION:

- The heterogeneity in late effect profiles, influenced by treatment modalities, individual risk factors and evolving therapeutic advances exposes the need for a personalized, risk-based approach to survivorship care.
- Effective LTFU programs must integrate comprehensive screening, patient education, and psychosocial support within a multidisciplinary framework to optimize health outcomes and quality of life.
- Nurse-led models of care, supported by evidence from diverse clinical contexts, offer a viable and potentially cost-effective strategy to enhance survivor engagement and adherence without compromising clinical safety.

THANKS FOR ATTENTION