Parameters, Considerations and Modulation of Physical Exercise Programs for Oncologic Patients – A Systematic Review

EXERCISE AND SPORTS MEDICINE CLINIC

REVIEW ARTICLE

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ABSTRACT

Introduction: This investigation searched for data that would describe the use of physical exercise, not as preventive method, but as a supporting therapeutic modality in the coping of the cancer (CA) and its treatment from diagnosis to recovery, since there is massive harm and side effects experienced by the patients that can be modified through the practice of physical exercises. Objective: To identify and select references which demonstrate necessary parameters for prescription of physical exercise programs to oncologic patients. Method: The systematic model of research was used in the Medline, Liliacs and Pubmed databases, using the terms: cancer, physical exercise, physical activity, exercise, being considered articles published between 1997 and 2008, in the Portuguese, English, Spanish and German languages. The articles that presented data which supported the use of physical exercise as a therapeutic method, as well as its modulation, indication, contraindication and interaction with other treatments were selected. Results: In the revised literature, subsidies that ground the use of physical exercise in its supporting role in the coping of CA and its treatment, as well as, benefits, indications, contraindications and precaution in the use of physical exercise were found. Conclusions: In spite of being a broad field where there is still a lot to be researched, if the contraindications and precautions are respected, physical exercise becomes safe, viable and effective for patients and survivors, giving them support to face the treatment and accelerate recovery.

Keywords: cancer, physical exercise, physical activity, exercise.

INTRODUCTION

The prevention effect that physical exercise primarily and secondarily develops in the evolution of many types of cancer (CA) is already well-reported. Currently, there are many investigations which have examined physical exercise in the prevention of Ca; however, little is known about the use of physical exercise during the treatment.

Although physical exercise does not directly reduce the risk of CA remission or delay the growth of the tumor, it is the key-component for the control of triggering factors[1] such as obesity, overweight, hormonal and immune alterations and physical inactivity, among others.

CA and its treatment cause deep alterations in the psychological and physical aspects of its patients. Although the treatments for CA are increasingly more efficient and modern, these alterations still compromise the quality of life and capacity of the patients in facing the treatment. These alterations vary according to the severity of the treatment, and sometimes place the individual in an extreme passive and hopeless condition.

Therefore, physical exercise constitutes an interesting therapeutic modality due to its improvement in physical capacities as well as the correlated ones which are crucial for supporting the diagnosis until recovery.

The literature available on the issue stresses the several benefits which physical exercise promotes in this population; however, broader information spread, clarification and knowledge from the part of the population and health professionals on this important instrument in the treatment assistance.

METHOD

Systematic research was used on the Medline, Liliacs and PubMed databases, using the terms: cancer, physical exercise, physical activity, exercise, individually and combined in citations in the title or abstract. The articles considered were published between 1997 and 2008 in Portuguese, English, Spanish and German.

112 references were obtained in this research, and 22 were selected for having presented data which supported the use of physical exercise as a therapeutic method, as well as its modulation, recommendation, contraindication and interaction with other treatments in oncologic patients.

RESULTS AND DISCUSSIONS

Effects of CA and its treatment

CA, and especially its treatment, result in severe collateral effects in the different body systems[2] causing physical, psychosocial and economical damage [3] which drastically reduce quality of life and functionality of the individuals[4].

The diagnosis of CA is a strong impact, reduces life expectancy and increases depression level in about 25% of the patients, being depression also related to the use of corticosteroids used in the treatment[2].

During the course of the treatment, the patients experience

many collateral effects, which include: astenia, ataxia, anemia, anxiety, nausea, vomiting, diarrhea, sarcopenia, osteopenia, mood swings, neutropenia, body composition and perceotion alteration, thrombopenia, decrease in flexibility, sleep disorders, self-esteem reduction, depression, cardiopulmonary and vascular function reduction, pain and fatigue[5-7], and these effects can persist for months or even years after the end of the treatment[5,8].

In the middle of the collateral effects, fatigue is undoubtedly the commonest[9-11] and most evident, affecting over 75% of the patients immediately after the first cycle of chemotherapy[8]. It is defined as a subjective state of oppression and prolonged exhaustion which decreases physical and mental capacities to perform work and which is not alleviated with rest[8].

Until some years ago, fatigue was seen by patients and doctors as a natural consequence of the disease and their treatment and not as something possible to be controlled[8]. Fatigue can present central etiological factors, such as: decrease in the gonadotropin level, increase of the number of circulating T lymphocytes, increase in the interleukin antagonist receptors, increase in the type II receptor of the soluble tumor necrosis factor, increase in the neopterin and peripherals level: negative energetic balance, disease and its treatments, systemic infections, hypothyroidism, malnutrition, metabolic disorders, sleep disorders, psychological factors[12]. Additionally, the following hypotheses can occur: anemia, ATP, vagal afferent and of the interaction of the hypothalamus – hypophysis/cytokines and 5HTaxis (serotonin deregulation)[8].

Besides its influence on the organic systems, fatigue negatively influences on the course of the treatment for affecting the patients[8] capacity to comprehend and retain information and for being a limiting factor for some therapies such as interferon and interleukin[9].

Due to the cardiorespiratory decontioning caused by CA and its treatment, increase of the metabolic rate, increase in the energetic cost, substantial increase of HR and lactate concentration in low intensity activities are observed[3], which cause the patients into avoiding exertion, which produces additional conditioning losses and lead to a cycle of self-perpetuation of fatigue[9]. This scenario is very harmful, since this cardiorespiratory deconditioning resulting from inactivity is a key-predictor for higher mortality rate in oncologic patients[7]. However, fatigue derived from causal factors (treatment, disease, detraining, sedentary habits) can be attenuated with the use of physical exercises and break this self-perpetuation cycle (figure1).

Some drugs are used to fight fatigue, such as megestrol acetate, modafinil and erythropoietin, to name some; however, these drugs are not efficient against muscular and cardiorespiratory losses[3].

According to the National Comprehensive Cancer Network (NCCN), physical exercise is one of the non-pharmacological interventions most efficient in the fatigue treatment[13], preventing, minimizing or decreasing it[7], besides promoting positive adaptations to the CA stress as well as the effects of its treatment during and after the therapies[14].

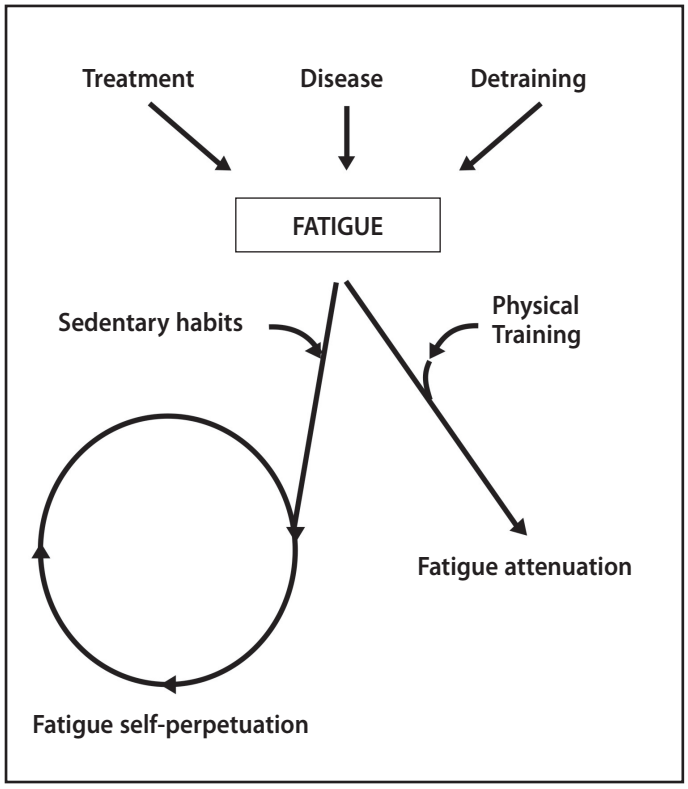

Figure 1. Fatigue self-perpetuation cycle[20].

When to use it

The implementation of a physical exercises program can be done in any of the three phases after the CA diagnosis[2]; however, in each phase their aims and consequent modulation are distinct.

Pre-treatment: comprehends the period between the disease diagnosis and the beginning of the treatment. The aims are focused on (a) improvement of the general functional status, (b) prevention and attenuation of the functional decline during treatment, (c) assistance to the individual to emotionally and psychologically face the disease while waits for the treatment[15]. The individuals who already practice some physical activity should priorize maintenance and the non-practitioners should progressively engage in a program.

- Maintenance of muscular mass and strength[2];
- Maintenance/optimization of the cardiorespiratory function[2];
- Maintenance of ADM[2];
- Optimization of immune function[2].

During treatment: the focus on this phase will be on patients who are experiencing treatment, regardless of its nature (surgical, chemo, radio, hormone, immune therapy and transplant). The aims are (a) to attenuate the collateral effects[5] and toxicity of the treatments, (b) to maintain the physical functions and body composition, (c) to maintain/improve functional capacity and muscular strength[4], mood status and quality of life, (d) to facilitate the treatment conclusion, and (e) to boost the efficiency of the treatments[15].

- Pain[2];
- Fatigue/anemia[2];
- Muscular weakness[2];
- ADM deficit[2];
- Balance and coordination[2];
- Lymphedema/edema/swollenness[2];
- Peripheral neuropathies[2];
- Osteopenia/osteoporosis[2];
- Myopathy induced by steroids[2].

Post-treatment: the approach this time will be focused on the survivors, that is to say, the individuals who have finished the tre-

atment, being exercise essential in the recovery process as well as optimization of the general health status and quality of life [15].

- Improvement of body composition[2];
- Improvement of muscular endurance and strength[2];
- Improvement of cardiorespiratory fitness[2];
- Improvement of flexibility[2];
- Improvement of physical function[2].

The aim is to return to the pre-diagnosis physical levels[2], to reduce the risk of remission and onset of other diseases, to develop exercising habits and to extend survival rate with quality[15].

Women and men during treatment have successfully participated in physical exercise programs, although the main study focus had been women with breast CA[16]. Exercise has been used in patients with prostrate, colon, lung, stomach, endometrial, head and neck CA, lymphoma, myeloma, melanoma and bone marrow transplant. In the majority of the studies, the recruited patients are on stage I or II of the disease; however, the few investigations carried out with patients in advanced stages or with metastasis have reported success[3,13].

Exercise types

The methodological choice as well as exercises typification to be used for these individuals is complex due to the extreme heterogeneity of the disease as well as to the no-linear response to exercise[2]. Due to the exercise particularity and complexity, a multidimensional approach which included resistance and aerobic exercises, relaxation, body awareness, massage and flexibility would be broader, since it would provide a more holisti approach[6,17,18].

Although it is not known yet which approaches are more efficient over others[19], the massive majority of the investigations use aerobic exercises of moderate intensity as a therapeutic method[3-5,10,16,18,20].

All investigations performed, each one with different samples, projects, interventions, periods and evaluation methods, report statistically significant results or in the improvement of physical aspects or in the reduction of collateral effects[4,5,18].

Therefore, the method as well as the modulation to be used should be carefully chosen, based on the daily needs of the patient[2].

Benefits

Recent studies and reviews suggest that intervention with physical exercise for patients and survivors have shown favorable results in all four domains related to quality of life (physical, physiological, psychological, social and spiritual)[4,13,14,16,19,21]. The related benefits include: fatigue reduction, improvement in quality of life, psychological wellness, body image, improvement in physical function (oxygenation capacity, cardiovascular and respiratory fitness, flexibility and general health status), anthropometric measurements (weight, fat mass and waist-hip index), biomarkers related to health (blood pressure, heart rate, hemoglobin concentration, hormones circulating levels and immunological parameters[7,14,16,18,22]. Besides these parameters, other very important ones are decrease of hospitalization time[9,18,20] and reduction of amount of analgesics used due to the increase of the painful threshold as well as release of endorphins[10].

It is important to highlight that, despite all benefits, very few patients exercise after the CA diagnosis and, out of the ones who exercise, great part does of in an inefficient and unsuitable manner[2].

Risks

Although moving is natural to humans, it is not risk-free[2], both for healthy individuals and for the ones experiencing some pathology. Some clinical precautions are necessary due to the treatment, namely: immunosuppressive potential, probability of fractures, cardiotoxicity exacerbation caused by chemo and radiotherapy, pain, nausea, fatigue and incapacity of tolerance [5].

However, according to the American Cancer Society (2007), the physical exercises interference in the conclusion of the treatment or efficiency of chemotherapy is unknown, and there are not physiological reasons of great concern concerning the application of exercise during the treatment[1].

In a study with over 700 patients, during several treatments, there was no report of any main adverse effect[5].

Strong evidence suggests that physical exercise is safe and efficient during CA treatment, improving physical functions and many aspects related to quality of life[1,14].

Conditions for prescription

In order to suitably prescribe exercises, it is necessary that the program follows some basic principles which structure any kind of training, both for healthy and sick individuals.

This situation is not different for individuals diagnosed with CA; however, besides the traditional principles of training (biological individuality, adaptation, specificity, reversibility and overload), another very important principle should be incorporated[2]. This principle, termed principle of modification[2], is necessary doe to the patient's response to the chemotherapy agents and other therapeutic devices used which momentously alters his/her physiological condition[2,11].

Other parameters to be considered in the prescription are: type and stage of the disease, medical treatment used, treatment intensity and duration, past and current physical exercise history and comorbidity conditions[5].

Additionally, the physiologists involved in the exercises prescription for this group of individuals should deeply understand about the CA physiopathology under consideration and the types of treatment which have been applied[13].

Besides approaching physiological aspects, it is crucial that the exercises are pleasant and interactive so that the development of new abilities and trust bonding can be developed with the patient[5] (table 1).

Contraindications and precautions (table 2)

Protocol

There is no direct evidence of the type, frequency, duration, intensity or ideal progression of exercises for this population[2,5,11]. The application will depend on the aims, health status of the patient and the CA; however, no kind of exercise is harmful to patients under treatment[13] (table 3).

Table 1. Strategies in the treatment of cancer and recommendations of physical activity[11].

Surgery System	Importance	Physical Activity Recommendation
Joint/muscle	Incision areas, sectioned muscles, muscles can be partially or totally removed. The reconstructed area may be sore and tense.	Before surgery, keep muscle strength to aid in recovery. Demand from patient to get off bed immediately after surgery. Before surgery, stretch the area which be affected to aid in flexibility. Progressively start (exercises on the bed) a one-two week program after surgery or after medical consent.
Lymphatic system/harm to the lymphatic system	If lymphocytes are removed, there may be some importance in the short and long run concerning lymphedema and infection.	Progressive exercises, increasing ROM, facilitating draining through the activity of a bomb, compression (area where the lymph nodes were removed), starting after medical consent. Incorporate diaphragm breathing and passive, isometric exercises within a few days after surgery.
Neurological	Neuropathy, numbness, space notion loss, nervous damage of the incision.	Moderate movement of the limbs to facilitate mobility. Breathing and relaxation techniques may help in the awareness sensation. Emphasis on balance exercises for stability.

Chemotherapy	Collateral Effects	Symptoms	Physical Activity Recommendation
Cardiovascular	Cardiomyopathy and pulmonary restriction	Palpitation, arrhythmia, short breath, swollen legs, exhaustion, alteration in blood pressure, vertigo.	Aerobic capacity may be compromised, intermittent exercises are recommended. Kind of activity may vary (walking, cycling, swimming). Start the exercise program in a progressive way. Whenever change the body position from sitting to laid or standing, slowly move to decrease vertigo and dramatic alterations of blood pressure. Rest may compromise blood pressure, pulmonary function as well as bone density, it is recommended to get off bed and move.
	Reduction in the blood red cells	Anemia Fatigue	Aerobic capacity may be compromised, intermittent exercises are recommended. Heart rate during the activity should be low or moderate 40% to 60% of maximum heart rate. Start exercise when appropriate in a progressive way. Keep self respiratory patterns according to the exercise.
	Reduction in the blood white cells	Suscetibility to infection	It is recommended not to participate in contact sports to diminish risk of injury. Wash hands before and after using the equipment. Start exercise whenever appropriate in a progressive way.
	Low platelets counting	Risk of hemorrhage. Sprain	Avoid contact sports and other activities which may result in cuts and sprains.
Neurological	Peripheral neuropathy	Paresthesia, burning, weakness, hand and/or foot numbness. Other symptoms associated with the nerves include loss of balance, restlessness, difficulty in picking up objects and buttoning clothes, walking problems, jaw pain, hearing loss, stomachache, constipation.	Maintenance of the extremities movements (toes and fingers). Move toes and fingers some times a day. Is balance sense is affected, falls can be avoided by carefully moving, using handrails to climb up and down stairs and use bath rugs in the tub and shower. Perform balance exercises with emphasis on the lower limbs associated with maintenance of central stability.
Gastrointestinal	Nausea, vomiting, mucositis, loss of appetite, constipation, diarrhea.	May limit the eating and absorption capacity of the needed nutrients.	Energetic decrease may make it difficult to perform sustained activities. Intermittent activities are recommended. Prolonged activities may be uncomfortable if diarrhea is present. Global physical activity may help in digestion and excess removal if constipation is present.
Other	Hair loss, thin and brittle nails, skin rash	Redness, itchiness, flaking, dryness and acne. Nails may become darker, fragile and chip and develop vertical lines or bands. Some people report they feel as if they got a cold from a few hours to days after chemotherapy. Cold symptoms (muscular soreness, headache, fatigue, nausea, low fever, cold, may last from one to three days.	In a cool day, wear a jacket to keep body temperature. Wear sun protection when walking or cycling outdoors. Care when using weight and exercise equipment when the skin and annexed are compromised. Skin rash should not affect activities such as cycling walking, swimming; however, pools treated with chlorine may irritate the skin. When cold symptoms are present, work within the possibilities at the moment.

Chemotherapy System	Collateral effects	Symptoms	Physical Activity recommendation
Gynecological	Anticancer drugs may damage the ovaries and reduce its hormone production. As a result, some women have their menstrual cycle irregular or completely interrupted during the chemotherapy period.	Chemotherapy may cause menopause symptoms as heat flushes and itchiness, vaginal burning or dryness.	Keep physical activity level to maintain muscle mass and cardiorespiratory conditioning. Perform activities with weight sustaining to promote bone health (any activity with feet on the ground, such as walking, climbing up stairs, dancing). Emphasize chest, thorax and abdomen strengthening. Improve posture. Relaxation techniques may help to face the heat flushes and other menopause symptoms.
Radiotherapy System	**Collateral effects**	**Symptoms**	**Physical Activity Recommendation**
Localized	Head and neck: hypothyroidism, esophageal mucositis. Thorax: cardiac toxicity. Pelvic area:complications in the bladder, vaginal and gastrointestinal tissues, hematuria.	Some symptoms are mainly felt after some weeks from radiotherapy. In some cases, the beginning of the collateral effects may not appear after some years.	Aerobic capacity may be compromised; hence intermittent exercises arerecommended. Heart rate during the activity should be from low to moderate (40%-60% from maximum). Initiate whenever appropriate, progressively. Avoid impact activities due to the bladder. Maintain self breathing pattern suitable to the exercise. Range of motion in the radiated area may get compromised. However, the area should be carefully mobilized to increase mobility.
Skin	Short-time alterations on the skin; long-time (six -10 months), skin thickness.	Itchiness, dryness, redness, heating, discomfort.	Hydrate the dry area (according to medical orientation), and protect skin when manipulating exercise equipment. The radiated area may become tense and with limited range of motion. Work progressively to maintain mobility. Perform exercise in ventilated places to prevent overheating. Drink plenty of water. Wear loose clothes to decrease skin rash.
Lymphatic	Scar formation of the lymphedema or sking burns.	Lymphedema	Improve lymphatic circulation with diaphragmatic breathing. Isometry, squeeze hands or pumping exercise. Use light weight to progressively strengthen the upper extremity of the body.
Transplant System	**Collateral Effects**	**Physical Activity Recommendation**	
Stem cell/bone marrow transplant	Affects white cells, red cells and platelets	Start program three-four weeks after transplant, in bed, on a chair or standing. Perform walking or cycling on a cycloergometer in an intermittent way. Modify movements if the biopsy area is sore.	

Table 2. Contraindications and precautions for the exertion test and exercise application[2,20].

	Contraindications	Precautions and alterations
Factors related to the treatment	Day and 24h after-application of cytostatics. Before blood collections Severe tissue reactions of radiotherapy	Treatments which affect lungs and /or heart Ulcerations and mouth sores: avoid tests with buccal device
Pulmonary	Severe dyspnea, cough, breathlessness Thoracic pain increased by deep inspiration	Mild to moderate dyspnea: avoid maximal tests
Musculoskeletal	Bone pain, head and neck of recent origin unusual muscle soreness severe cachexia (loss > 35% of pre-treatment weight) Extreme fatigue Low functional status	Investigate pain or cramps Avoid high impact and contact exercises Myopaties induced by steroids Limit exercise intensity
Siystemic	Acute infections Fever < 38° general discomfort	Avoid exercises until the patient is asymptomatic for 48h Avoid high intensity exercises
Gastrointestinal	Severe nausea Vomiting or diarrhea in the last 24 to 36h Dehydration inadequate food and fluids ingestion	Follow-up with nutritionist
Cardiovascular	145mmHg systolic and 95mmHg diastolic Irregular pulse Swelling on the ankles	Risk for associated-cardiac disease Caution with excessive medication to control BP and HR Lymphedema
Hematological	Platelets < 50,000 white cells < 3,000 Hemoglobin < 9g/dL	Avoid risk of hemorrhage Avoid risk of bacterial infection (swimming pool) Avoid high intensity exercises
Neurologic	Significant decline in the cognitive status Vertigo/frivolous person Disorientation. Blurry vision. Ataxia	Cognitive alterations Lack of balance/peripheral sensory neuropathies

Table 3. Guidelines for exercise prescription[2,5,11,13,20].

Type	Exercises involving big muscle groups: cycling and walking are especially recommended for their safety and tolerability. Alteration Will be based on the treatments (surgery, chemotherapy and radiotherapy).
Frequency	At least three to five weekly times. Daily exercises for deconditioned patients.
Duration	At least 20 to 30 continuous minutes. For deconditioned patients or the ones experiencing collateral effects, perform interval training (sets of exercises with rest intervals).
Intensity	Moderate, dependent on the fitness level of the patient and the treatment. 50% to 75% $\dot{V}O_{2max}$/60% to 80% of HR reserve/ PSE between 11 and 14
Progression	It should be firstly done by the frequency and duration and later by the intensity. Slow and gradual for deconditioned patients or the ones experiencing collateral effects.

CONCLUSION

When the contraindications and precautions are respected, exercise becomes not only safe and viable[1], but also efficient for patients and survivors[11], positively affecting physical and psychosocial aspects, providing them with support to face treatment and its deleterious effects and, in post-treatment, accelerating recovery and extending their survival rate with quality.

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ERRATA

In the RBME Volume 17 # 1 – January/February in the article "Influence of the Ergometric Protocol in the Onset of Different Criteria of Maximum Exertion", on page 20, in Table 1 where it can be read (L+min-1) the correct should be (L.min-1) and in table 2, in columns PR1, PR2 and PR3 where set is read it should be 9.

Table 1. Physiological and metabolic responses in the three investigated protocols.

	PR1		PR2		PR3	
$T_{exhaustion}$ (min)	11 ± 1	(9-14)	10 ± 3	(6-15)	24 ± 3**	(17-30)
P_{max} (Watts)	183 ± 57	(135-325)	153 ± 29	(125-225)	182 ± 43	(120-250)
$VO2_{max}$ (L.min-1)	2.68 ± 1.0	(1.48-4.53)	2.58 ± 1.0	(1.47-4.81)	2.99 ± 1.3	(1.63-5.60)
HR_{max} (bpm)	168 ± 15	(141-195)	165 ± 12	(153-186)	180 ± 13	(159-200)
[Lac]	6.4 ± 1.6	(4.0-8.2)	5.3 ± 2.6	(1.8-9.3)	8.1 ± 2.3*	(5.1-11.3)

Mean ± standard deviation (minimum and maximum values); Texhaustion, time of exhaustion; P_{max}, maximum power reached; VO_{2max}, oxygen maximum uptake; HR_{max}, maximum heart rate; [Lac], blood lactate concentration at the end of the test; *significant difference for $p \leq 0.05$; ** significant difference for $p \leq 0.01$.

Table 2. Onset frequency of the different criteria of maximum exertion in the evaluated protocols.

	PR1	PR2	PR3
Plateau (≤ 150 mL.min-1)	05/9	01/9	0/9
HR_{max} (≥ 95%)1	01/9	0/9	03/9
[Lac] (≥ 8.0 mM)	02/9	01/9	06/9
RER (≥ 1.1)	06/9	07/9	04/9

1 HR_{max} = 220 – age; Number of occurrences/total of observations; the abbreviations follow format of table 1.