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Reviews

Ways to improve the medical surveillance in shift workers

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Abstract

Metabolic syndrome is a common condition among shift workers (but not exclusively), as this type of work produces changes in the circadian rhythm associated with changes in glucose and lipid metabolism and an increased risk of cardiovascular disease.

During the employment or periodic examinations, the occupational medicine doctor performs certain tests such as electrocardiogram, blood pressure measurement, orders blood tests (glycemia, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamine transpeptidase (GGT), creatinine, depending on the type of exposure of the worker. Their changes can translate into restrictions of some activities, the need to re-organize work and, in extreme cases, the unfitness for the respective job.

That is why it is necessary to find effective methods for the early identification of the risk of developing metabolic syndrome among workers regardless of the type of work or schedule they perform, before the onset of a chronic disease that can lead to an impaired quality of life and/or a reduction of work capacity. This article reviews the definition of metabolic syndrome, the current recommendations introduced in international guidelines and some of the screening methods which may be useful for the the medical surveillance of workers at risk of developing metabolic syndrome.

Keywords: *night shift work, metabolic syndrome, cardiovascular disease*

Introduction

Romanian legislation defines the legal time of work, shift work and night work, and the legal benefits for night workers [1-3]. In real life, some workers have a working schedule that includes more than 5 consecutive night shift days or more than 8h per day and 40 h per week, thus with shorter rest periods. Other employees have a constant program that starts at 4 in the morning or ends at 12 at night without being considered night shift workers according to the legal definition.

These work-related hazards are present all around the world. For example, more than 15% of the European workforce have long working hours per week (> 48h per week), 10% to 15% of the individuals work in their spare time [4]. The Eurofound and International Labour Organization report pointed out that 10%

to 40% are shift workers and 10% to 20% are night workers, with women preferring shift work, while men preferring night work, probably due to social economic factors and family dynamic [4].

Night shifts or irregular shifts trigger circadian rhythm disruption, which has numerous negative effects on health. A prospective study published in 2020, analysed a cohort of 12850 individuals (participants in the Screening Across the Lifespan Twin study – SALT study) exposed to night work and their risk of mortality. This study reported that night work is associated with a higher risk of mortality due to all causes in workers with at least one night shift per month for more than 6 years, compared to those not exposed. The specific mortality due to circulatory diseases or to cancer was also increased. The conclusion was maintained after adjusting for sex, age, education, coffee and alcohol consumption, smoking, body mass index (BMI), severity of disease at baseline, occupational group (white versus blue-collar), and leisure-time physical activity [5]. A study on a cohort of 5775 Taiwanese hospital workers reported an increased risk of developing metabolic syndrome (OR =1.40 [1.06, 1.85]; p <0.02) and high waist circumference (OR= 1.44 [1.17, 1.78] p<0.01) in night shift workers compared to day shift workers, independent of number of night shifts, as well as a high risk of elevated blood pressure (OR=1.15 [1.01, 1.31], p<0.04) in workers with a higher number of night shift work [6].

Another consequence of night shifts is insomnia. A recently published meta-analysis reported an important association between insomnia and the incidence of myocardial infarction no matter the limit of 5 years of insomnia, less or more. Relative risk for people who sleep less than 5 hours a day is 1.56, 95% CI = 1.41–1.73, compared with those who sleep 7-8h per day. It also identified a RR= 1.69, 95% confidence interval [CI] = 1.41–2.02, p < .00001 for persons with insomnia versus persons without [7]. Other meta-analysis outlined that insomnia is bidirectional associated with elevated blood pressure [8] and that patients with insomnia have a higher risk of high blood pressure, hyperglycaemia, hyperlipidaemia and obesity [9].

View of all the above data it is not surprising that in large cohort studies, night shift was also related to the development of the metabolic syndrome [6, 10] as this syndrome is currently accepted as a synthesis of risk factors for cardiovascular diseases, diabetes, chronic renal disease, non-alcoholic fatty liver disease, and several forms of cancer. The association with night shifts is common; in this respect, a systematic review calculated an OR = 2.17 (CI = 1.31–3.60) in night shifts compared to daily workers [11]. Therefore, we will focus on the cluster of risk factors which define the metabolic syndrome, the current recommendations of prevention and the possible relations to the occupational medicine practice.

Definition of the metabolic syndrome

The metabolic syndrome definition includes central obesity (estimated by the waist circumference), the high blood pressure (BP), the level of basal glycemia, and two components of the lipoprotein profile [12].

World Health Organization defines obesity as "abnormal or excessive fat accumulation that presents a risk to health" [13] and World Obesity Federation defines it as "a chronic, relapsing, multifactorial disease" [14]. Central obesity based on the abdominal circumference better relates to the metabolic consequences of obesity than the definition built on the body mass index. The abnormal values for waist circumference in Caucasians are ≥ 94cm for men and ≥ 80cm for women. As there are more and more migrant workers under the occupational medicine surveillance programs, the specific threshold for these workers should be checked. For example, for workers from Asian origin, the threshold values are ≥ 90cm in men, and ≥ 80cm in women.

The International Diabetes Federation (IDF) defines high BP as a systolic BP is ≥130 mmHg and/ or a diastolic BP is ≥85 mmHg. These limits are in line with the updated guideline issued by the European Society of Hypertension (ESH) in 2023, which classifies values between 130-139/85-89 as "high normal" and recommends life style intervention and treatment in grade I hypertension (140-159/90-99 mmHg), even with low-moderate cardiovascular risk [15]. It is important to underline that these criteria for metabolic syndrome also refers to the already treated high BP, no matter the level of the BP measured during the office visit.

There are two lipoproteins which are included in the diagnosis of the metabolic syndrome: the serum triglycerides >150mg/dL and the HDL cholesterol< 40/mg/dL (men) and 50 mg/dL for women. As for treatment of dyslipidaemia, it is also among the recognized criteria of diagnostic [12].

Fasting glycemia >100 mg/dL or an already diagnosed diabetes mellitus are another component of the metabolic syndrome. If fasting glycemia is modified, there is a need to check for the ≥ 8h of fasting before the blood sample collection, the exclusion of any acute diseases ("stress hyperglycaemia") and

the medication. The most frequent drugs causing an increase in glycemia are drugs used for lowering the BP (thiazide diuretics, certain beta-blocking agents), the lipid-modifying agents (statins, nicotinic acid) [15], antibiotics (fluoroquinolones), anti-viral drugs (protease inhibitors), anti-fungal (pentamidine), anti-epileptic (phenytoin and valproic acid), bronchodilators (theophylline), hormones (glucocorticoids, growth hormone, somatostatin analogues), oral contraceptives (high doses of oestrogen) [16], antipsychotic (mainly olanzapine, clozapine) [17], anticancer agents (e.g., L-asparaginase, or mammalian target of rapamycin (mTOR) inhibitors [18] or immunosuppressive agents (calcineurin inhibitor) [19]. Many of these drugs could also interfere the lipid metabolism or favour weight gain, increasing the chance for metabolic syndrome.

Some of these clinical findings or laboratory test are recommended for medical surveillance in relation to exposure to different occupational risk factors and could serve to calculate the risk of developing cardiovascular diseases. During the annual visit, the occupational medicine doctor should also record any chronic treatment followed by the workers and evaluate the possible interference with the blood test results of the metabolic syndrome or of the mandatory blood test monitoring for exposure to occupational hazards. For example, statins treatment for dyslipidemia, could rise the blood level of ALT, AST or creatin-kinase. High levels need a differential diagnosis with chronic hepatic diseases in those exposed to hepatoxic hazards. Caution should be taken not only to the higher incidence of type 2 diabetes (a minimum of 2 extra cases in 1000 individuals, for every 1 year of therapy) [20] in an already high-risk population due to night shifts but also on low BP effect, which might predispose to work accidents [21].

Current recommendations

In the context of general prevention, the individual cardiometabolic risk evaluation is beneficial for all workers and especially for those whom these conditions would later become a possible restriction of activity.

a) Obesity

Even though there are persons with obesity, but without metabolic disorders, it is important to remember that these individuals have a 60% higher risk of major cardiovascular event (comparing with healthy persons without obesity) and, for them, the cardiovascular factor risk is more rapid developing [22].

The first therapeutical step in diabetes and hypertension is life style intervention, e.g., weight management by the adherence to a healthy diet and an increase in exercise. In order to prevent obesity, caloric restriction through eliminating snacking during the night, for night workers [23] or having the same meal hours as day workers [24] have a protective effect on the cardiometabolic risk [25-27]. In a recent systematic review, several night shift workers were considered: fire fighters, medical personnel, casino workers, miners [28]. The most frequent barriers to be addressed for an effective weight reduction intervention in night shift workers were: personal related factors such as stress, time constraint due to workload or other personal commitments with minim or no time for physical activity, work and organizational factors (e.g. lack of routine for food intake, lack of healthy food options during the working time, irregular work), and also general socio-cultural factors such as lack of healthy food options and adequate promotion of a healthy diet. From the analysis of the results, the authors concluded that without a proper management of these factors, the effectiveness of interventions on weight reduction in night shift workers have limited chances of success.

b) Diabetes

Diabetes Standard Care, published in January 2023 [29, 30], recommends that every healthcare professional should be involved in screening for diabetes, meaning that occupational medicine physicians (OMPs) should also be included. Measuring the blood glucose is regularly performed for night workers. In some national legislations, including the Romanian one, glycemia should also be measured in those exposed to electrical field, non-ionizing electromagnetic fields, ionizing radiation, high temperature, professional drivers, rescuers, security agents, persons who work in isolation and at height, mainly for the characterization of the risk for accidents related to acute diabetic complications without proper treatment or organizational changes (access to food, possibility to administer treatment, colleague support etc). In these circumstances, working night shifts will be a significant contributor to the personal risk and measures should be taken accordingly. Higher risks have been reported also in exposures to volatile aromatic hydrocarbons [31], arsenic [32], tungsten [33], styrene and ethylbenzene exposure [34], cobalt and molybdenum [35] and need further confirmation for the inclusion in the standard medical surveillance.

Beside the occupational hazards, the non-

occupational risk factors should be identified by the medical history and the clinical examination in night shift worker. There is a consensus that having a first-degree relative with diabetes, women with a history of gestational diabetes or who have delivered child greater > 4 kg, sedentarism and the presence of other comorbidities: acanthosis nigricans, polycystic ovary syndrome are major risk factor for type 2 diabetes [36].

Having the comprehensive picture of the risk, OMP has a privileged position in the early diagnosis of diabetes and should comply in his surveillance programs to the international recommendations.

c) Cardiovascular risk

Circulatory diseases represent more than one third of the total cause-specific work-related deaths in 2019 in Europe [37]. Stress at work (imbalance between high effort and low reward, violence and bullying, long working hours, irregular working hours or exposure to dust, fume, vinyl chloride, carbon disulfide, lead are the most frequently factors considered [38-40]. Reduction of this high rate is primarily based on job intervention but also on the early identification of relevant biomarkers for the cardiovascular risk and appropriate treatment. Concerning night shifts, recommendations for fewer consecutive night shifts, sufficient shift intervals, and shorter night shift duration has been proposed [41]. This should be even more relevant for the ones with high cardiovascular risk defined by the European Society of Cardiology (ESC) which states, that screening for cardiovascular risk should begin for asymptomatic persons after the age of 40 years, using the SCORE system [42]. Identifying the workers at risk (Familial hypercholesterolemia, family history of high cholesterol levels and/or environmental risk) and providing them with advices on healthy life style would help those individuals retain their jobs in the future. Also, the persons with high or very high risk of developing cardiovascular diseases should be considered priority for follow-ups [42].

SCORE system identifies the risk of developing fatal cardiovascular diseases (CVD) in 10 years based on the status of smoker/non-smoker, sex, total cholesterol and systolic blood pressure. The risk is considered low if <3, moderate, if 3-4, high if 5-9 and very high if ≥10. It is necessary to specify that there are factors (family history of cardiovascular disease men<55 years, women<60 years; obstructive sleep apnea; atrial fibrillation; HIV infection, etc.) that modify this system, upgrading the result to an upper level of risk, making it difficult to clearly classify cardiovascular disease risk [42]. So, it became a priority to develop other tools for better screening.

Lately, ESC provided an application for risk calculating, easy to use from a smartphone or online from a laptop/PC [43]. These calculators use more specific test results, such as non-HDL cholesterol, triglycerides, hemoglobin A1C (HbA1C). There are lifetime risk calculators and up to 10 years risk calculators, for individuals with or without diabetes, with or without previous cardiovascular disease (Table 1) [44]. These are personal risk profiles. Romania, Moldova, Bulgaria, Lithuania, Belarus, Latvia, Serbia, Montenegro, Ukraine, are classified as countries with populations at very high risk.

Practical issues

a) Obesity

As mentioned above, not only the BMI, but also the content in adipose tissue and its distribution are very important. Obesity Medicine Association recommends calculating the body fat percentage as another way to estimate obesity [45]. There are different ways such as Multi-Compartment Models (the Gold Standard), Air Displacement Plethysmography (Bod Pod), Hydrostatic Weighing to identify the total content in adipose tissue in the human body. These are more expensive tests and are not used for screening, but mainly for research purposes. Normal values (in percentage from the total body mass) are less than 32% for women and less than 25% for men [46].

The US Army Body Fat Calculator is the most accessible, tool. It uses sex, height, weight, age, neck circumference and waist circumference in the calculation. This calculator is accessible online for free, taking into account that measurements should respect the following anatomical landmarks [47]:

•the neck circumference: just below the level of larynx (Adam's apple),

•the male's waist circumference: at the level of the navel (belly button),

•the female's waist circumference at the point of minimal abdominal circumference

•for women only: plus, the hip circumference where the buttocks protrude backward the most.

b) Rapid tests

The rapid tests are a plus in workers with diabetes, dyslipidemia or cardiovascular diseases, but might be used also for screening in the workplace if the device and method is internationally validated. The main advantages of this type of measurement are the easiness of usage, the fast results (maximum 5 minutes) and no special measures for deposit of the

kits. On the market, beside the well-known glucose analyzers, many others, FDA and CE approved, are available such as analyzers for creatinine, ALT, AST, GGT, cholesterol and its fraction, triglycerides, HbA1C and others. Some devices are dedicated to a specific test, and others devices provide results for several blood biomarkers. These last ones might be of more interest for the OMPs, as out of a single blood drop and a strip they may provide a complex information, such as glycaemia, triglycerides and cholesterol or creatinine, uric acid and urea, for example.

c) BP and cardiac rhythm monitoring

High blood pressure (HBP) is another component of the metabolic syndrome and might be a life-threatening condition in contrast with the job's requirements.

Ambulatory blood pressure monitoring (ABPM) is useful to identify both the effect of work (if any) on the blood pressure and the efficiency and/or compliance to treatment. The monitoring is generally applied for 24h, but might be extended to longer periods. Comparison during one working day and free days could identify differences and is a strong argument for the recommendation of changes in the workplace, scheduling or work activities. Meantime, in night shift workers, the "dipper" status might be modified by the working schedule and interpreted accordingly.

Screening for arrhythmias is another example of action an OMP would be able to do in ambulatory monitoring and helps in a proper fitness for work evaluation. Nowadays, smartwatches are able to measure BP or to record ECG for more than 30 seconds. They can screen for some specific arrythmias (atrial fibrillation, tachycardia), or just identify an irregular rhythm. When detected, a notification is signaled to the person that wears the device. There are smartwatches that do both BP and arrythmia detection. Some of these wearables are approved by the FDA and/or CE and these should be the preferred selected ones. Limitations in the usage of these devices are due to cost, flexibility in setting the recording time. Type of recording, namely the position of the device, motion of the hand or of the whole body could also create differences in data and difficulties for comparisons.

ESC and EHRA (European Heart Rhythm Association) also recommends the use of smart patch ECG devices, with 1 to 3 leads which is FDA and CE approved [48]. Some are single use only (developed during the Covid-19 pandemic crisis), having a recording range from 24h to 30 days, depending on the device. The price might be a barrier, even for the most affordable ones. A collaboration with the treating cardiologist is always recommended in order to adjust, if necessary both work factors and medical treatment.

Conclusions

From all the above, several conclusions emerge: first, the OMPs can advise workers according to the findings of the test results in order to prevent diseases related to the metabolic syndrome. Second, OMPs could propose a larger panel of tests to identify the cardiometabolic risk, in particular in those exposed to occupational cardiovascular hazards, including night shifts. The high-risk workers should be target of preventive interventions to manage this risk in order to maintain health and their current job position. Third, the integration of the occupational risk factors to the care provided by the general practitioners and other medical specialists would allow a better management of workers with cardiometabolic disorders.

Table 1. Estimation of the cardiovascular risk

Prediction algorithm	Defined Outcome	Tests included in the risk calculation	Other elements included in the risk calculation	Targeted population, exclusion criteria
SCORE2	10 years risk of CVD	Systolic blood pressure, total cholesterol, HDLc	Age>40, sex, smoking status	Apparently healthy < 70 years; No previous CVD or type 2 diabetes mellitus
SCORE2 Diabetes	10 years risk of CVD	Systolic blood pressure, total cholesterol, HDLc, HbA1c, eGFR	Age>40, sex, smoking status, age at diabetes diagnosis	For persons with DM type 2
SMART risk score	10 years risk of CV event	Systolic blood pressure, creatinine, hss CRP, total cholesterol, HDLc, LDLc	Age>30, sex, smoking status, years since 1st CV event, type(s) of atherosclerotic vascular disease, antithrombotic treatment	For persons with previous CVD (it was developed in a population with mostly type 2 DM patients)
SMART-REACH model	Lifetime risk & treatment effect	Systolic blood pressure, creatinine, total cholesterol, LDLc	Age>45, sex, Geographic region, smoking status, type(s) of atherosclerotic vascular disease, dyslipidaemia treatment, antithrombotic treatment	For persons with previous CVD
DIAL	Lifetime risk & treatment effect	***The DIAL algorithm is currently under scientific revision to correct issues***		For persons with DM type 2
LIFE CVD*	10 year & lifetime risk & CVD-free life-expectancy	Systolic blood pressure, BMI, total cholesterol, HDLc, LDLc	Age>35, sex, smoking status, geographic region, type(s) of atherosclerotic vascular disease, dyslipidaemia treatment, antithrombotic treatment, parental history of MI prior to age 60	Apparently healthy No previous CVD

*For myocardial infarction, stroke or vascular death and event free life-expectancy if standard care is provided

The table is a synthesis of the ESC, Association for Acute CardioVascular Care, European Association for Palliative Care and Association of Cardiovascular Nursing & Allied Professions guidelines.

Legend: CVD = cardiovascular disease; HDL c= high density lipoprotein cholesterol; LDLc- low density lipoprotein cholesterol; HbA1c = glycated haemoglobin; eGFR= estimated glomerular filtration rate; hssCRP= C-reactive protein; BMI= body mass index; MI = myocardial infarction

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