Electrocardiographic Changes and Work-related Stress – a Cross-sectional Study in a General Working Population

Master thesis in Medicine

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Abstract

Background: Work-related stress described by the job strain and effort-reward-imbalance models has been associated with increased cardiovascular risk. However, the evidence is not sufficient. Atrial fibrillation, LBBB (left bundle branch block), prolonged QTc and resting heart frequency are electrocardiographic markers of cardiovascular disease. If they could be linked to job strain and effort-reward imbalance it would add plausibility to an association between these models and an elevated cardiovascular risk.

Aims: To explore the relationship between job strain and effort-reward imbalance and atrial fibrillation, LBBB, QTc and resting heart frequency demonstrated with resting ECG, with the general aim of giving a further basis for the evidence connecting work-related stress with an increased risk of cardiovascular disease.

Methods: This cross-sectional survey investigated randomly selected men and women in Västra Götalandsregionen (n=1,552 and 1,094 in two different samples). Information about effort-reward imbalance, job strain and ECG parameters was collected during the period 2001-2004 as part of the INTERGENE/ADONIX research project. The regression models were adjusted for gender, age and current smoking.

Results: No significant association was found between prolonged QTc and work-related stress. There were too few cases of atrial fibrillation and LBBB to allow for statistical analyses. In the adjusted model heart frequencies $\geq 90^{th}$ percentile were significantly inversely related to job strain (OR 0.65, 95% CI 0.44-0.96). For heart frequencies $\leq 10^{th}$ percentile there was an inverse but non-significant association (OR 0.73, 95% CI 0.49-1.09).

Conclusions: No electrocardiographic parameters could be significantly, positively associated with job strain or effort-reward imbalance. The inverse relationships between job strain and high and low heart frequencies possibly indicate a reduced risk of cardiovascular disease. This finding is controversial, however, due to a lack of support from other studies and the limited ability of this study to ascertain causality.

Key words: Work-related stress, job strain, effort-reward imbalance, ECG.

Background

Job strain and effort-reward imbalance

There are several models to describe work-related stress. The most extensively studied is the demand-control model or job strain model developed by Karasek in 1979. This postulates that the combination of high psychological demands and low decision latitude at work results in mental strain and a stressful condition with the risk of developing stress-related diseases [1]. More precisely, Karasek subdivided the situation at work into four categories (fig. 1) describing different levels of strain from psychological demands and decision latitude [2] (pp 31-43). Decision latitude here refers to the combination of skill discretion and autonomy, or simply “control” [2] (p 58).

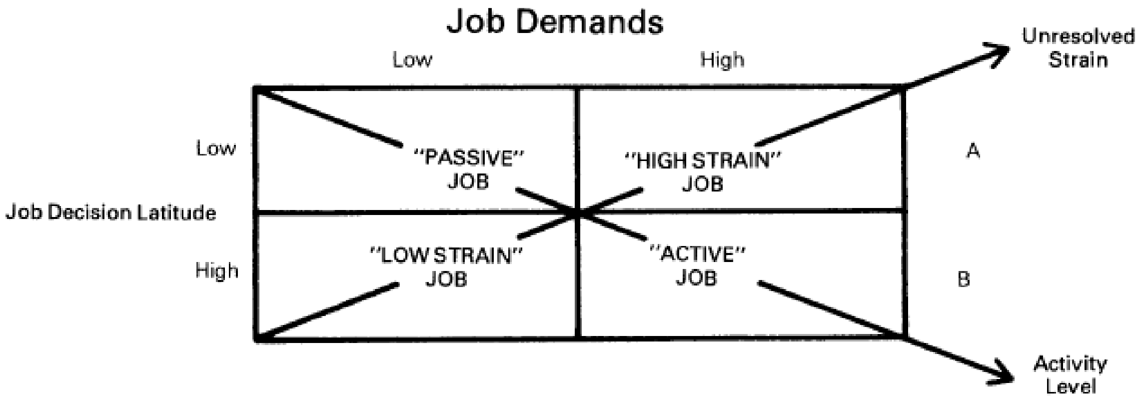

Fig. 1 The job strain model [1]

1. Low strain is defined as low psychological demands and high control, for example the case for many natural scientists, which produces a relaxed state and a healthy situation at work.
2. Passive refers to low psychological demands and low control, giving a working situation at risk of inducing impaired problem-solving capacity and atrophy of learned skills and abilities.
3. Active jobs have high psychological demands and high control, for example physicians. Karasek hypothesizes that this situation gives positive psychosocial outcomes such as learning and new behavior patterns both on the job and outside of it.

4. High strain is described as high psychological demands combined with low control. Karasek proposes that this creates a situation equivalent to being exposed to a danger that one cannot manage. The arousal that arises as a part of the fight-and-flight response cannot be translated into action, leading to residual strain and the risk of developing psychological and physical illness [1, 2]. Further on we will refer to this category as “job strain”.

There are various questionnaires that can be used to estimate job strain; the Job Content Questionnaire, developed by Karasek in 1985 [3] has probably been the most widely used [4]. The recommended version contains a total of 49 Likert-scaled questions regarding, for example, decision latitude, psychological demands and job insecurity [5]. Based on this, a common way of defining job strain is a score above the median or mean on demands combined with a score below the median or mean on decision latitude, where the median or mean is collected from the study population or a reference database. However, other formulations that omit the segment of the strain population closest to the population mean – reducing the risk of misclassification – are used as well [4].

Another well-known model used to describe work-related stress is the effort-reward imbalance model, introduced by Siegrist in 1986 [6] and described in detail in 1996 [7]. The effort-reward imbalance model has undergone some modifications over time but according to the current version three important concepts can be identified: effort, reward and overcommitment (fig. 2) [8]. Effort and reward are “extrinsic” factors where “effort” refers to the demands and obligations placed on the worker and “reward” includes the three different occupational gratifications: money, esteem and status control (e.g. promotion prospects and job security).

Siegrist predicted that an imbalance between these two concepts, in terms of high efforts spent and low rewards received – also referred to as non-reciprocity between costs and gains – would evoke negative emotions which would in turn activate the sympathetic nervous system. A sustained autonomic arousal would lead to a risk of adverse health effects [7, 8]. Effort and reward can be studied separately from overcommitment.

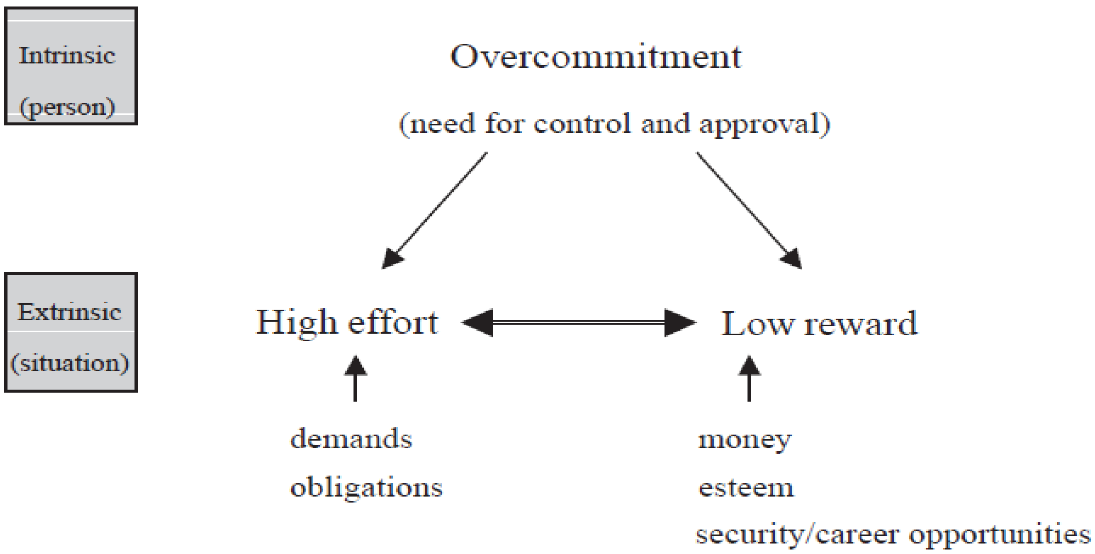

Fig. 2 The effort-reward imbalance model [8]

Overcommitment is an "intrinsic" factor complementing the model. An overcommitted person has unreasonably high ambitions and a strong need for control and approval on a personal level [8]. This personal characteristic is thought to trigger the perception of non-reciprocity between costs and gains at work (people with this characteristic will have a tendency to always work too much) and consequently – in accordance with the reasoning above – increase the risk of poor health. The model expects the strongest effects on health when extrinsic effort-reward imbalance and overcommitment coexist [9].

In scientific research, effort-reward imbalance is measured with self-report data using the Effort-Reward Imbalance at Work Questionnaire with psychometric scales for effort, reward and overcommitment [10]. As in the Job Content Questionnaire, each scale contains several Likert-scaled items scored 1 to 5, giving a discrete value on each variable. Calculating the ratio between the sums of the scores of “effort” and “reward”, compensating for different numbers of items with a correction factor, gives a measure of the effort-reward imbalance. A ratio above 1 is often defined as an effort-reward imbalance, but the ratio can also be used as a continuous variable with or without log-transformation [10-12].

Associations with the risk of cardiovascular disease

There is today a variety of data indicating an association between work-related stress and an elevated risk of cardiovascular disease. In a systematic review from 2004, eight of seventeen longitudinal cohort studies, six of nine case-control studies and four of eight cross-sectional studies showed significant positive results between job strain and an elevated risk of cardiovascular disease defined as fatal or non-fatal coronary heart disease, myocardial infarction, angina, diagnosed ischemic heart disease or self-reported angina pectoris in the different studies [13]. Three longitudinal studies showed positive but non-significant results. Relative risks and odds ratios in the studies with significant results ranged from 1.21 to 4.0 (95% CI 1.1-14.4 in the latter) in the longitudinal, 1.45 to 2.3 in the case-control and 1.5 to 2.46 in the cross-sectional studies. The internal validity of the included studies was generally high, but biases towards the null dominated, especially in the longitudinal studies, indicating an underestimation of the effects of job strain and a stronger association than presented. However, because the data for women was sparse, this evidence concerned mainly men.

Similar results were presented by Backe et al. in a systematic review including only prospective cohort studies [14]. In seven of thirteen cohorts treating job strain and in all three cohorts applying effort-reward imbalance, a statistically significant elevated risk of developing cardiovascular diseases was shown. The rest of the studies showed positive but non-significant results. Outcomes in the majority of the studies were overall cardiovascular disease or coronary heart disease, but some studies investigated only stroke, angina pectoris or hypertension. At least one study with positive significant results was represented for each outcome. As for the systematic review mentioned above, no conclusions could be made for women due to insufficient data. Thus, moderate evidence for an association between both of the models and an increased risk of cardiovascular disease among men was found, but the authors stated that more confirming research was needed, especially for the effort-reward imbalance model, which was used in only three cohorts.

Further, in a meta-analysis from 2006 including fourteen prospective cohort studies – ten on job strain and four on effort-reward imbalance (of which two were from the same cohort but with slightly different approaches) with a total of 83,014 and 11,258 employees respectively – Kivimäki et al. calculated an age- and gender-adjusted relative risk of cardiovascular disease on 1.43 [95 % CI 1.15-1.84] for job strain and on 1.58 [95 % CI 0.84-2.97] or 2.52 [95 % CI 1.63-3.90] for effort-reward imbalance, depending on which of the two studies from the same cohort that was included in the meta-analysis [15]. The outcomes were the same as above with the addition of aortic aneurysmal rupture, heart failure and sudden death in one study. Again, it is important to note that only three independent studies examined effort-reward imbalance and therefore the results should be taken with some caution. Also, regarding job strain the relative risk decreased to 1.16 [95 % CI 0.94-1.43], that is no longer statistically significant, after adjustment for cardiovascular risk factors such as smoking, hypertonia, body mass index and others. The authors state that this can be interpreted in two different ways: Either the factors adjusted for are confounders, meaning that job strain is only a risk indicator rather than an actual risk factor, or they are intermediate factors in the association between job strain and cardiovascular disease.

In yet another systematic review of 33 prospective or case-control studies, Eller et al. found moderate evidence indicating high psychological demands, but not job strain, as a risk factor for definite coronary heart disease among men [16]. Here, the term “definite coronary heart disease” contained the endpoints angina pectoris, acute myocardial infarction, cardiovascular or coronary death and sudden death. There was not enough evidence to associate effort-reward imbalance and ischemic heart disease and the data on women was again too sparse to draw any conclusions.

An update to this review from 2014 placed special focus on the statistical power of the analyses [17]. Of 169 significance tests in 44 different papers, only ten tests in two papers had a ≥80% power to detect a rate ratio of 1.2, or in other words a 20% increased risk of definite coronary heart disease. In seven of the analyses the power exceeded 95%. Even if the required excess risk had been 40%, merely ten additional analyses would have had sufficient power. This finding indicates that the studied populations on the subject have generally been too small to ensure a clear relationship between work stress and cardiovascular disease.

In the largest of the two studies with sufficient power, Kivimäki et al. conducted a meta-analysis of 13 independent cohort studies investigating job strain – three published and ten unpublished – with a total of 197,473 participants of which half were women [18]. The outcome was incident coronary heart disease defined as the first non-fatal myocardial infarction or coronary death. After adjustment for sex and age a positive significant association was seen between job strain and an increased risk of incident coronary heart disease [HR 1.23, 95% CI 1.10-1.37]. The association was weaker in unpublished studies [HR 1.16, 95% CI 1.02-1.32] than in published ones [HR 1.43, 95% CI 1.15-1.77], indicating publication bias. Thus, because previous reviews have included only published data, there is a possibility that they have overestimated the risk. However, the study was somewhat limited since it was not based on a systematic review.

In summary, the evidence is moderate. To date, no conclusions about causality can be made, but the data is pointing in the direction that job strain is in fact a risk factor for cardiovascular disease as a whole. For the effort-reward imbalance model the data is insufficient and somewhat contradictory. Additionally, data on women is not as comprehensive as on men. We can state that more confirming research is needed. A well-established correlation is important to form the basis for implementation of preventive actions in workplaces in the future.

One problem has been that there are great differences in study design, for example in the measurement of exposure, which has made it impossible to conduct meta-analyses in several of the systematic reviews [13, 14, 16] and has also hampered the possibility of conducting the larger multicentre studies needed to achieve enough power in the analyses. Performing such large studies with standardized methods could help in validating the association seen in the existing data [17]. However, another way to achieve this is to investigate the association between job strain and effort-reward imbalance and established risk factors and biological or clinical markers for cardiovascular disease. Such an association would make it biologically plausible that there in fact is a relationship between work-related stress, as expressed by the two models, and cardiovascular risk. Additionally, it would shed light on the etiologic mechanisms of this association.

Many studies have already been presented on this issue. For instance, job strain has been significantly associated with obesity [19, 20], physical inactivity, diabetes [19] and smoking [19, 21] in several large meta-analyses of cross-sectional data. Some studies also indicate associations between job strain and effort-reward imbalance and atherosclerosis [22, 23].

Work-related stress and electrocardiographic changes

This study investigates the relationship between work-related stress and changes in the resting electrocardiogram (ECG) – a well-established clinical marker of cardiac disease. No previous studies have been published on this topic. Yet, we identify four ECG parameters of interest in this context:

Atrial fibrillation is one of the major risk factors for ischemic stroke with a prevalence of 2.9% in the adult population ≥20 years and of 0.6% in the adult population <60 years (that is, the prevalence increases with age) in Sweden, based on patient registers [24]. As indicated earlier, stroke has been significantly associated with job strain in men but not in women [14]. However, only a small number of studies, all with methodological limitations, have investigated the relationship between work-related stress and stroke and some studies have null findings, making the evidence uncertain and inconsistent [25, 26]. An association with atrial fibrillation would help resolve these uncertainties and support a positive association between stroke and work-related stress.

Left bundle branch block (LBBB) is a conduction defect in the heart where a blockage of the impulse spreading in the left bundle branch gives a characteristic ECG appearance. In a study of an Icelandic general population aged 33 to 71 years, the prevalence was 0.43% for men and

0.28% for women [27]. Another study has reported the prevalence 0.4% in 50-year old Gothenburg men, increasing to 2.3% at the age of 75 [28], but the exact prevalence in a Swedish general population is uncertain. LBBB is virtually always a sign of underlying heart disease. The most common causes are acute or previous myocardial infarction, although LBBB is also seen in cardiomyopathies, congenital heart defects, hypertensive heart disease and valvular defects [29] (p 190). Hence, LBBB is a good objective indicator of heart disease which might be useful in creating firmer evidence of the association between work-related stress and cardiovascular disease and providing information about underlying mechanisms.

The QT interval is an electrocardiographic parameter measured from the beginning of the QRS complex to the end of the T-wave. Thus, it reflects the de- and repolarisation of the ventricle [30]. A prolongation of the QT interval known as the "Long QT syndrome" can be either hereditary or acquired, where the acquired form is assigned to drug side effects, electrolyte imbalances and more, and increases the risk of a polymorphic ventricular tachycardia called Torsades de pointes. This can progress to ventricular fibrillation and sudden death [29] (pp 238-240) [31]. Because the QT interval is dependent on heart rate, a heart rate corrected QT (QTc) is used when measuring the QT interval [29] (p 240). There are different formulas developed for this purpose and therefore the reference values for QTc vary depending on what formula is being used. A common way of defining prolonged QTc is >450 ms for men and >470 ms for women based on Bazett's formula ($QTc=QT \times (HR/60)^{1/2}$), which has been most widely used [29, 31, 32]. QTc is longer in women than in men because of a shortening of the QT interval in males after puberty [33]. The risk of serious arrhythmias increases the longer the QTc is [29].

Meloni et al. have shown an elevated risk of a borderline or prolonged QTc (430-450 ms and >450 ms respectively in this study) among male shift workers compared to daily workers [34]. Similar results with significantly higher adjusted odds ratios of long or prolonged QTc among male shift workers compared to daily workers have been reported in two studies by Murata et al., but long and prolonged QTc were here defined as ≥420 ms and ≥440 ms respectively – that is not pathological [35, 36]. Two studies have presented no association between shift work and QTc prolongation, making the evidence divergent [37, 38]. Nevertheless, an association between job strain and effort-reward imbalance and QTc prolongation would still be an interesting subject of investigation, especially since there is some evidence linking shift work to low decision latitude and high cognitive demands [39]. A positive finding could provide a pathophysiological link between the risk of sudden death due to cardiovascular disease (used as an outcome in some of the studies included in the previously mentioned systematic reviews) and work-related stress.

Finally, several prospective cohort studies have reported significant associations between a high resting heart rate or an elevation of heart rate over time and an increased risk of coronary heart disease death, cardiovascular death and/or all-cause mortality [40-43]. Two of the studies actually classified high resting heart rate as an independent risk factor [40, 42]. The associations are strongest for the most extreme heart rates above 80-90 bpm, but increasing risks for heart rates above 65 bpm have also been described [43]. One prospective cohort study has also shown that low heart rate <60 bpm compared to 60-69.5 bpm in healthy men in a general population increases the future risk of cardiovascular events (the aggregate risk of myocardial infarction, stroke and sudden death) after adjustments for multiple cardiovascular risk factors [44]. Finding an association between psychosocial work variables and resting heart rate could therefore provide important support to the evidence linking these variables to an increased cardiovascular risk.

Further, it is known that resting heart rate is highly dependent on the inflow of sympathetic and parasympathetic activity to the heart. High resting heart rate has accordingly also been shown to be associated with increased sympathetic activity [45]. An autonomic imbalance in terms of increased sympathetic and/or decreased vagal activity has been related to a number of conditions, including cardiovascular diseases [46]. Interestingly, by studying heart rate variability, such an autonomic imbalance – visible as decreased heart rate variability – has been associated with both job strain and effort-reward imbalance, although the evidence is somewhat contradictory [47]. Hence, a relationship between elevated heart rate and the two models would also strengthen the evidence that autonomic imbalance is a possible pathophysiological link between work-related stress and cardiovascular disease. This would also be in accordance with the hypotheses made by the two models.

Therefore, this cross-sectional study aims to examine the relationships between four electrocardiographic parameters and two well established models of work-related stress in a general population. We claim that exploring these relationships can strengthen the epidemiological evidence associating work-related stress with cardiovascular disease and add to the knowledge about etiologic mechanisms. Our hypothesis is that atrial fibrillation, LBBB, prolonged QTc and high and low resting heart frequency are positively associated with job strain and effort-reward imbalance.

Aims

Specific aim: To explore the relationship between work-related stress, measured as job strain and effort-reward imbalance, and atrial fibrillation, LBBB, QTc and resting heart frequency, demonstrated with resting ECG, in a general working population.

General aim: To give further basis for the epidemiologic evidence connecting work-related stress with an increased risk of cardiovascular disease.

Scientific issue

- Are job strain and effort-reward imbalance positively associated with atrial fibrillation, LBBB, prolonged QTc and high and low resting heart frequency demonstrated with resting ECG?

Methods

Population and data collection

We performed a retrospective cross-sectional cohort study where the subjects were recruited from the data register of the INTERGENE and ADONIX research projects. INTERGENE is a population-based study exploring the INTERplay between GENEtic susceptibility and environmental factors, life-style, etc. and the risk of cardiovascular diseases [48]. ADONIX (Adult Onset Asthma and Nitric Oxide) is a subproject within this study focusing on asthma [49]. The data collection was carried out from April 2001 until the end of 2004 – that is, we used only previously collected data – and the study population consisted of coronary heart disease cases, their first-degree relatives and randomly selected controls in Västra Götalandsregionen [50]. Only the randomly selected sample participated in our study. General procedures in the studies were as follows: The participants were mailed study information, a questionnaire and an invitation to a basic clinical examination where they also received complementary questionnaires containing questions on, among other things, the psychosocial situation at work [50]. Altogether, 8,625 subjects were invited [49] and the response rate was 3,614 men and women aged 25-74 years. Detailed information about the INTERGENE and ADONIX research projects is available at http://www.sahlgrenska.gu.se/intergene/.

Since our study demanded information on electrocardiographic changes and psychosocial work variables, all subjects with missing (n=382) or incomplete (n=5) ECG and all subjects not currently working full- or part-time or with missing information on this issue (n=1,222 of the remaining 3,227) were excluded. Further, we excluded all subjects that did not fill in the psychosocial questionnaire (n=379 of the remaining 2,005). From the remaining 1,626 subjects, two subsamples were made. In the first sample, which we will refer to as the "job strain sample", all subjects with missing or incomplete information on demand and control variables (n=74) were excluded leaving 1,552 subjects, 752 men and 800 women. In the second sample, which we will refer to as the "effort-reward sample", all subjects with missing or incomplete information on effort and reward variables (n=532) were excluded leaving 1,094 subjects, 544 men and 550 women. The two samples were analyzed separately.

Variables

Electrocardiography

A standard 12 lead resting ECG was used for the electrocardiographic measurements. The participants rested for five to ten minutes and jewelry was removed before registering. Limbs were lying freely. A Siemens Megacart utilizing the Glasgow Royal Infirmary Interpretive ECG Algorithm was used to read the ECGs. It can be argued that manual interpretation of ECG provides greater validity compared to computer reading. However, due to the great number of ECGs and the limited time available, manual interpretation was not possible. The selected parameters for the purpose of this study were heart frequency, atrial fibrillation, left bundle branch block (LBBB) and heart rate corrected QT interval (QTc). QTc was automatically calculated with Hodges formula: QTc = QT + 1.75 x (Heart rate - 60) where QT and heart rate were measured by the ECG algorithm. There is no consensus about preferred reference values when using this formula. However, two large studies of 10,303 and 13,354 normal ECGs in men and women are of interest. Both studies set the 98th percentile as the upper limit, that is, the top 2% were considered prolonged. One study suggested 454 ms for men and 460 ms for women as upper limits [51]. The other study presented reference values based on age and gender. For ages 20-69 years, which are approximately the same ages as for the population in our study, the upper limits were 440-450 ms for men and 448-456 ms for women [52]. We therefore chose to define prolonged QTc as > 450 ms for men and > 460 ms for women as probable relevant limits.

Psychosocial work variables

Information about psychosocial work variables was collected from the questionnaires about the psychosocial situation at work filled in at the clinical examination.

Demand and control

Demand and control were explored using a questionnaire with three Likert-scaled items for each variable **(see appendix)**. The questionnaire has previously been used by Söderberg et al. [53]. Even though it differs from Karasek’s Job Content Questionnaire [3] it describes similar aspects of the working situation and can be considered applicable to the job strain model. Each item was scored 1 to 5. A high score indicated high demand or high control respectively for the particular item. The scores were summed, giving a discrete value between 3 and 15 for each variable. The median score was 10 for demands and 11 for control. A score above or equal to the median was defined as “high control” or “high demands” respectively, while a score below the median was defined as “low control” or “low demands”. Two categories were created for the statistical analyses, labeled “job strain” (high demands/low control, equal to “high strain” in Karasek’s model) and “no job strain” (high demands/high control or low demands/high control or low demands/low control, equal to “active”, “low strain” and “passive” in Karasek’s model).

Effort and reward

To examine effort-reward imbalance, the Effort-Reward Imbalance at Work Questionnaire [10] was used **(see appendix)**. The questionnaire contains five or six items on effort and eleven items on reward. One item evaluating physical effort is recommended for inclusion “…only where prevalence of physical workload is part of the typical task profile” [10]. A previous study on the INTERGENE and ADONIX cohort has reported that their effort-reward sample consisted predominantly of white-collar workers [53]. In our sample, a majority of the subjects (69.5%) reported no physical strain. Consequently, the item measuring physical load was excluded and five effort items were used.

All items were scored 0 to 4 but rescored as 1 to 5 before the statistical analyses. The summing of effort items resulted in sum scores between 5 and 25 with a median on 12. Higher scores indicated higher effort. The sum scores for reward ranged between 12 and 55 with a median on 50. Before summing, all reward items were inverted so that higher scores indicated higher reward. To evaluate the effort-reward imbalance a ratio (ER ratio) between the sums of the scores was created compensating for different numbers of items with a correction factor: ER ratio = $\sum_{\text{Effort}}/(\sum_{\text{Reward}} \cdot (5/11))$. Inverting the scores for reward results in the highest ratio for subjects reporting high effort and low reward, that is, a higher ratio indicates a greater imbalance between effort and reward. The ratio varied between 0.2 and 2.32. Effort-reward imbalance was defined as an ER ratio > 1 while an ER ratio ≤ 1 was defined as balanced or “no effort-reward imbalance”.

Smoking

A yes or no question was asked to determine whether the participants currently smoked cigarettes. This resulted in the two categories: “current smoker” and “not current smoker”.

Statistical methods

Statistical calculations were performed with IBM SPSS Statistics for Windows, Version 20.0. Dichotomous categorical variables for job strain and effort-reward imbalance were created with categories as described above. In all regression analyses “no job strain” and “no effort-reward imbalance” were used as references. Linear regression analyses were performed with heart frequency and QTc as dependents. For each variable, one model was unadjusted and one model was adjusted for gender, age and current smoking as possible confounders. Age was used as a continuous variable, and gender and current smoking were dichotomous variables with “female” as reference for gender and “no” as reference for current smoking.

To evaluate the distribution of heart frequencies in the different samples, two different categorical variables dichotomized by the 90^{th} and 10^{th} percentile respectively were produced. Prevalence odds ratios for job strain and effort-reward imbalance were calculated for heart frequencies above or equal to the 90^{th} percentile and for heart frequencies below or equal to the 10^{th} percentile. P-values were calculated using chi-square tests. Additionally, a multiple logistic regression analysis adjusted for gender, age and current smoking was performed for the job strain sample. The variables for gender and current smoking were used in the same way as for the linear regression analyses. Age was converted to a categorical variable with five categories: age < 30 years, age 30-39 years, age 40-49 years, age 50-59 years and age ≥ 60 years, and was used as a dummy variable with the lowest category as reference. Logistic regression analysis was not considered necessary for the effort-reward sample due to the very weak associations for the prevalence odds ratios.

The Pearson correlation, R, and R^2 were calculated between the ER ratio as a continuous variable and heart frequency and QTc respectively. Adjustments were made for gender, age and current smoking in the same way as for the linear regression analyses. Finally, prevalence odds ratios for “any ECG change” – defined as atrial fibrillation, LBBB or prolonged QTc – and prolonged QTc with stratification for gender were calculated. In both of these cases categorical variables dichotomized into “yes” or “no” were created. Chi-square tests were used again to generate p-values.

All linear and logistic regression analyses were also stratified for gender. Naturally, no adjustments were made for gender in these analyses. All tests were double sided and a p-value < 0.05 was considered significant.

Power calculations

Power calculations were performed with SAS, version 9.2 for Windows. Since the size of the study population was given beforehand and was not possible to change, we chose to calculate the power of our study based on the received proportions of job strain and effort-reward imbalance in the different samples and the approximated prevalence of prolonged QTc, atrial fibrillation and LBBB from the reference literature (mentioned previously) [24, 27, 28, 51, 52]. 456 of 1,552 subjects reported job strain and 91 of 1,094 subjects reported effort-reward imbalance.

Approximated prevalence of ECG parameters:

- Prolonged QTc: 2%
- Atrial fibrillation: 1%
- LBBB: 0.5%

The significance level in the calculations was 5%. Based on this, the powers to detect a significant doubled risk – due to the low prevalence numbers we considered this relatively high increase in risk to be clinically relevant – for the different ECG parameters were as follows:

- Prolonged QTc: 60% power in the job strain sample and 30% power in the effort-reward sample.
- Atrial fibrillation: 37% power in the job strain sample and 22% power in the effort-reward sample.
- LBBB: 24% power in the job strain sample and 18% power in the effort-reward sample.

Thus, the power to explore these parameters was low or very low.

In contrast, the power to detect a significant doubled risk of high and low heart frequencies ($\geq 90^{th}$ or $\leq 10^{th}$ percentile) was high in the job strain sample – 99% – and acceptable in the effort-reward sample – 75%. Although the prevalence was higher in this case we chose to keep a doubled risk in the calculations for comparison.

Ethics

In this study, data from the previously performed INTERGENE and ADONIX research projects has been used. All participants gave informed consent to be included. The methods and approaches have been approved by the regional ethical review board at Gothenburg University (application number Ö092-91 for ADONIX and Ö237-2000 for INTERGENE). We used the data only for statistical analyses. Therefore we did not consider there to be any ethical issues in our study.

Results

Tables 1 to 3 show characteristics of the original cohort before exclusions, the job strain sample and the effort-reward sample respectively. Mean age was considerably higher in the original cohort – 51.4 years compared to 46.0 years in the job strain sample and 46.2 years in the effort-reward sample. Notable here is that the mean age of those not working full- or part-time, who were excluded, was 59.4 years. 456 of 1,552 subjects (29.4%) reported job strain and 91 of 1,094 subjects (8.3%) reported effort-reward imbalance (ER ratio > 1). Compared to men, a larger percentage of women experienced job strain or effort-reward imbalance, with a particularly large difference for job strain. Further, women presented a higher mean heart frequency and mean QTc than men in all categories in both of the samples.

There were 30 cases of atrial fibrillation and 26 cases of LBBB in the original cohort. However, the majority of those disappeared during the exclusion. Only one case of atrial fibrillation and job strain and no cases of atrial fibrillation and effort-reward imbalance were seen. In total, there were only five cases of atrial fibrillation in the job strain sample and four in the effort-reward sample, which were too few for any further statistical analyses. This was also the case for LBBB, where only six cases were detected in both samples.

Linear regression analyses did not display any significant association between job strain or effort-reward imbalance and heart frequency or QTc (tables 4 and 5). The strongest association was seen between job strain and heart frequency in the unadjusted model including all subjects (95% CI -0.22 to 1.94 with p-value 0.12). Adjustments for age, gender and current smoking, however, weakened this association substantially (95% CI -0.73 to 1.43 with p-value 0.53).

The Pearson correlation (R) between the ER ratio as a continuous variable and QTc and heart frequency was -0.02 and -0.04 respectively after controlling for age, gender and current smoking (table 6). R^2 was 0.0004 for QTc and 0.002 for heart frequency.

Tables 7 and 8 present the association between heart frequencies above or equal to the 90th percentile (≥74 bpm) and below or equal to the 10th percentile (≤49 bpm) in the job strain and effort-reward samples respectively. All analyses in the effort-reward sample tested null. In the job strain sample there were no significant associations for the 90th percentile. However, the proportion of "job strain"-workers with heart frequencies below or equal to the 10th percentile were significantly lower than the proportion of "no job strain"-workers in these categories. The prevalence odds ratio was 0.63 with 95% CI 0.43 to 0.94 and p-value 0.02.

To explore this further, a multiple logistic regression model compensating for age, gender and current smoking was performed (table 9). The association disappeared for job strain and heart frequencies below or equal to the 10th percentile (95% CI 0.49 to 1.09, p-value 0.13). Additionally, in the logistic regression model a significant link between heart frequencies above or equal to the 90th percentile and job strain was detected (95% CI 0.44 to 0.96, p-value 0.03). After stratification this relationship was close to significant for women (95% CI 0.39 to 1.02, p-value 0.06) but not for men.

51 cases of prolonged QTc were found in the job strain sample – 14 reporting job strain and 37 reporting no job strain (table 10). No significant relationships could be discovered. 39 cases with prolonged QTc were found in the effort-reward sample – 35 with ER ratio ≤ 1, but only 4 with ER-ratio > 1, making the data insufficient for reliable statistical analyses.

Finally, the prevalence and prevalence odds ratios for “any ECG-change”, defined as prolonged QTc, LBBB or atrial fibrillation, were investigated (table 11). No significant associations were seen for job strain. The effort-reward data again was insufficient for reliable analyses – 4 cases with ER ratio > 1 and 43 cases with ER ratio ≤ 1.

Discussion

In this cross-sectional study we found a significant inverse association between high heart frequency, defined by the 90th percentile, and work-related stress described by the job strain model after adjustments for gender, age and current smoking. Low heart frequency, defined by the 10th percentile, was significantly inversely related to job strain, but the significance disappeared after adjustments for the mentioned variables. All analyses failed to detect any relationship between QTc and work-related stress. The cases of atrial fibrillation and LBBB were too few to allow for performing any reliable statistical analyses.

Methodological limitations

Design

The cross-sectional design of our study entails some important limitations. Firstly, the chronology of exposure and outcome is unknown, that is, conclusions about causality cannot be made. Secondly, we do not know anything about the time of exposure to work-related stress. We based our study on the fact that changes in ECG are clinical markers of cardiac disease. Cardiac disease develops over a long period of time. Hence, if a part of the subjects reporting work-related stress have only been exposed for a shorter time (which we do not know), it is possible that we have underestimated the risk of ECG changes.

Power

It is also important to note that more than half of the subjects in the original cohort were excluded. One consequence was that the mean age was considerably reduced. This can be referred to the fact that a large percentage of the excluded subjects were those not currently working full- or part-time. The mean age in this group was 59.4 years and most likely many were pensioners. Since the prevalence of atrial fibrillation and LBBB increases with age [24, 28], this is probably why most cases of these ECG changes disappeared during the exclusion.

As previously mentioned, the prevalence of atrial fibrillation in the adult population <60 years in Sweden is estimated at 0.6% [24] and the prevalence of LBBB in such a population is probably the same or slightly less although more uncertain [27, 28]. A general working population like ours will always consist of a great majority of people <65 years. Thus, the expected prevalence of atrial fibrillation and LBBB will be low.

Therefore the power of our study to detect significant associations (in the power calculations we considered a doubled risk to be relevant) between job strain or effort-reward imbalance and atrial fibrillation or LBBB was very low. In fact, too few cases were found for reliable statistical analyses and we have to state that our study was not sufficiently powered to explore atrial fibrillation and LBBB in a general working population. Larger studies are needed for this purpose in the future. This also applies to future investigations of the relationship between work-related stress and prolonged QTc, where the problem with low power was likewise considerable.

Measurements

Even for young samples like ours the prevalence of atrial fibrillation was very low – 0.32% (5 of 1,552 subjects) in the job strain sample and 0.37% (4 of 1,094) in the effort-reward sample.

One possible explanation is the use of resting ECG, which implies an obvious risk of missing subjects with paroxysmal atrial fibrillation, thus underestimating the number of cases. Using Holter registering in future studies could limit this problem.

Because of practical circumstances, all ECGs were computer read. We do not know the accuracy of the ECG algorithm used to detect LBBB and atrial fibrillation and to determine the QT interval compared to manual interpretation. Hence, the precision in the electrocardiographic measurements is unclear. Looking at other algorithms, 92.9% sensitivity and 99.8% specificity to detect LBBB [54] and 83.3% sensitivity and 99.1% specificity to detect atrial fibrillation compared to cardiologists [55] have been reported. The expected prevalence for both of the conditions was, as mentioned before, low, most likely below 1% [24, 27, 28]. For prevalence numbers between 0.5 and 1%, the above sensitivities and specificities would give positive predictive values between 70.0 and 82.4% for LBBB and between 31.7 and 48.3% for atrial fibrillation. Thus, the misclassification risk would be intermediate for LBBB but high for atrial fibrillation.

Concerning QTc, a ~10 ms difference of QT interval between two different ECG machine manufacturers has been reported in putatively the only study on this issue [56]. Further, from a sample with the Long QT Syndrome, great differences in the accuracy in detecting prolonged QTc between three different computerized measurements have also been shown (sensitivity between 40 and 90%) [57]. However, the same study also presented a considerable inter- and intra-reader variability in manual interpretation of the QT interval by four experienced observers. In another interesting study, 83-90% of arrhythmia experts (n=106) but merely 61-84% of cardiologists (n=329) were able to correctly measure the QT interval in four different ECGs [58]. Thus, both manual and automatic interpretations seem to have limitations. In view of this, although we must be cautious in making conclusions based on data from alternative computer programs, it is plausible to assume that manual interpretation by expert cardiologists would have substantially increased the precision of determining atrial fibrillation, while the extent to which the measurements of LBBB and QTc would have improved is unclear.

Another limitation lies in the choice of an alternative questionnaire to measure job strain. This will make direct comparisons with studies using the more commonly used Job Content Questionnaire [3, 4] difficult since we cannot rule out differences in the classification of job strain. This is especially true since our questionnaire is not validated, making it unclear how accurately we have actually measured job strain.

Analyses

Lastly, to avoid overcompensation we have chosen to be careful with compensating for cardiovascular risk factors since it cannot be ascertained from previous research that these are not intermediate factors in the association between work-related stress and cardiovascular disease [15]. At the same time, confounding effects cannot be excluded. It is therefore possible that compensation for factors such as hypertension and BMI would have given more accurate results.

The same reasoning leads to the conclusion that the choice to compensate for current smoking (as a cardiovascular risk factor) might be both an advantage and a limitation. However, if smoking actually is a confounder, it would have been more appropriate to include “number of years smoking cigarettes” and “number of cigarettes smoked per day” instead of just current smoking, since this would have allowed us to explore dose response effects. Still, current smoking is not irrelevant and has in fact been associated with elevated resting heart rate [59].

Methodological strengths

To measure effort and reward we used the standard Effort-Reward Imbalance at Work Questionnaire, which has been validated and shown to have scales with good or acceptable internal consistency and good discriminant validity [10]. Thus, for the effort and reward measurements the internal validity was higher and comparisons with other studies will be more reliable than for the job strain measurements.

Further, studies have shown advantages in using the ER ratio as a continuous or log-transformed continuous variable instead of a binary variable. Particularly in populations with low prevalence of effort-reward imbalance defined as an ER ratio > 1, the use of the ER ratio as a continuous variable, which takes into account all values instead of dichotomizing them into two categories, increases the statistical power [11, 12] . The prevalence in our sample was relatively low – 8.3% – as was the power. Thus, the fact that we complemented the analyses by using the ER ratio as a continuous variable when calculating the correlation with heart frequency and QTc must be considered a strength of our study.

Other advantages were that we investigated a randomized sample in a general population. This increases the external validity. In addition, both exposed and controls were collected from the general population, making the two groups highly comparable. We also used Hodges formula to calculate QTc. Compared to other formulas, Hodges formula has been shown to give QTc values with the lowest correlation to heart rate (looking at both sexes and all heart rate intervals at the same time) [51, 60]. Aiming to produce reliable QTc values, this is eligible since the purpose of the formulas is to correct for heart rate. In addition, one of the studies used the same ECG algorithm as the one in our study, making the result highly relevant.

Resting heart rate and job strain

As mentioned before, a high resting heart rate has been associated with an elevated cardiovascular risk in different studies [40-43] and is associated with increased sympathetic activity [45]. In contrast to our hypothesis we found that high resting heart rate, defined by the 90^{th} percentile (≥74 bpm), was significantly negatively associated with job strain after adjustments for gender, age and current smoking – that is, the opposite of the hypothesized positive association. There is also evidence indicating low resting heart rate to be associated with cardiovascular disease [44]. Calculation of prevalence odds ratio showed that low resting heart rate defined by the 10^{th} percentile (≤49 bpm) was significantly negatively associated with job strain, again in conflict with our hypothesis. However, the significance disappeared in the adjusted model (p-value 0.13).

Thus, our results actually seem to indicate that workers experiencing job strain have a decreased instead of an increased risk of cardiovascular disease and autonomic imbalance, contradicting previous research. However, it has to be taken into consideration that the evidence supporting the association between low resting heart frequency and an elevated cardiovascular risk so far is limited [44]. Additionally, some studies have presented positive associations between high resting heart rate and death from cardiovascular diseases but with great attenuation after adjustments for cardiovascular risk factors, suggesting high resting heart rate to be merely a marker of cardiovascular risk but not an independent risk factor [61, 62]. This makes the interpretation and relevance of the negative associations uncertain.

Further, we have already declared that the cross-sectional design of our study does not give any information about the chronology of exposure and outcome. Consequently, causality in the relationships found cannot be ascertained. There is also a lack of support from other studies associating high and low heart frequencies with job strain and the significant association with low heart frequency in our study can probably be assigned to confounding effects since no significance was seen in the adjusted model.

Therefore we cannot make any controversial conclusions from our results. What we can safely conclude, though, is that they support neither the epidemiological evidence connecting job strain and cardiovascular risk nor the possible association between job strain and autonomic imbalance.

Another important observation to mention in this context is the risk that the significant results are merely random findings due to mass significance. We did 40 significance tests with 0.05 as the critical significance level. If all the tests were independent, two false positive results should therefore be expected by chance (0.05 x 40 = 2). We had two significant results. However, if many analyses are performed on the same sample, as in our study, some of them will most likely not be independent, making the expected number of false positive results uncertain. Still, because of the large number of significance tests, we have to regard the risk of mass significance as imminent.

QTc

We found no relationship between work-related stress and QTc in our study. Although all regression analyses on both job strain and effort-reward imbalance indicated an inverse relationship and two of three prevalence odds ratios indicated a negative association between job strain and prolonged QTc (in men there was a non-significant positive association), the uncertainty of the estimates were generally very high. It is of course possible that larger studies with greater power will be able to show significant results. However, for effort-reward, the low linear correlation with QTc speaks against any such findings.

We calculated R^2, where R is the Pearson correlation coefficient, to 0.0004 for QTc and the ER ratio after controlling for age, gender and current smoking. R^2 is interpreted as the degree of explanation one variable has for another if causality exists. In other words, R^2 tells us how much of the variation of one variable is explained by another variable. Thus, if there is a causal relationship in this case, the ER ratio merely explains 0.04% of the variation in QTc. Yet, even though this indicates a lack of connection between the two variables, a nonlinear relationship of importance cannot be excluded from our results.

Although, to our knowledge, no studies have been published on the subject of work-related stress and QTc prolongation, there is some evidence associating low decision latitude and high cognitive demands with shift work [39], making it relevant to discuss previous studies reporting significant associations between male shift workers and prolonged QTc [34-36]. All of these studies utilized Bazett’s formula for heart rate correction. As stated before, Hodges formula has been shown to generally produce QTc values with the lowest correlation to heart rate and therefore probably give the most reliable values [51, 60]. Additionally, in the same studies Bazett’s formula was reported to give QTc values with the strongest correlation to heart rate (for the heart rates 40-100 bpm and 60, 80 and 100 bpm in the different studies) and therefore the authors concluded that this formula is inappropriate to use in most situations [51, 60]. Furthermore, the definition of long and prolonged QTc in two of the studies investigating shift work and QTc were ≥420 ms and ≥440 ms respectively [35, 36] instead of >450 ms, which is the more commonly used limit for men when using Bazett's formula [31]. These methodological limitations make the results uncertain and a positive association between shift work and prolonged QTc questionable – even more so when taking into account the two mentioned studies presenting no association [37, 38].

Assuming the association between work-related stress and shift work to be true, the implications that there could be an association between work-related stress and QTc are therefore weak. Our study presented null findings on both men and women and has the advantages of using an appropriate formula to calculate QTc and relevant definitions of prolonged QTc. Taking all this together, we claim there is no evidence to date indicating a positive association between prolonged QTc and work-related stress.

Suggestions for future studies

Since this was the first study exploring the relationships between work-related stress and ECG-changes, more studies are necessary to confirm or negate our results. For LBBB and atrial fibrillation there was a lack of power in our study. We were not able to provide any information about how these variables are associated with work-related stress. Larger studies are therefore needed in the future. This is also the case for prolonged QTc for which low power similarly was a major problem. In all cases, including resting heart rate, there is a need for longitudinal studies providing information about the chronology of exposure and outcome to increase the capability of determining causal relationships.

To improve internal and external validity, the Job Content Questionnaire and validated electrocardiographic measures need to be used. Especially for atrial fibrillation, Holter registering would be preferable. Compensating for cardiovascular risk factors as possible confounders in the statistical analyses should also be considered.

Conclusions

No significant positive associations were found between atrial fibrillation, LBBB, prolonged QTc or high and low heart frequencies and job strain or effort-reward imbalance. Therefore, this study could not provide any additional support to the existing evidence associating these psychosocial work variables with an increased risk of cardiovascular disease. The power to detect significant associations (doubled risk) between job strain or effort-reward imbalance and LBBB and atrial fibrillation in particular, but also prolonged QTc, in this general Swedish working population was low. Special attention should therefore be given to power calculations in future studies aiming to explore these variables' relationship to work-related stress in similar populations.

The finding of inverse relationships between job strain and high and low resting heart frequencies possibly indicates a reduced risk of cardiovascular disease for workers experiencing job strain. However, such an interpretation is controversial since high heart frequency might only be a marker of cardiovascular disease and few studies to date support the association between low resting heart frequency and increased cardiovascular risk. The finding in itself is also uncertain because of a lack of support from other studies and since causality could not be ascertained due to the study design. Further, the association with low heart frequencies was not significant after adjustments for gender, age and current smoking. More studies are needed before too far-reaching conclusions are made.

Our results do not change the fact that associations between psychosocial work variables and electrocardiographic changes are possible and might provide important support to established evidence connecting work-related stress and cardiovascular risk. Future studies will have to explore this further with the overall aim of building a well-founded correlation that can form the basis for implementation of preventive actions in workplaces.

Populärvetenskaplig sammanfattning

Mycket forskning bedrivs idag för att utreda hur stress i arbetet påverkar hälsan. Studier har redan visat att det kan finnas ett samband mellan arbetsrelaterad stress och en ökad risk för sjukdom i hjärta och kärl, till exempel hjärtinfarkt och stroke. Innan detta kan sägas med säkerhet behövs dock fler studier som bekräftar vad man hittills sett.

Två teoretiska modeller för att beskriva arbetsrelaterad stress dominerar i vetenskapliga studier. Den ena menar att höga krav i kombination med låg kontroll över arbetsuppgifterna leder till stress i arbetet. Den andra föreslår istället att om arbetet kräver en stor ansträngning samtidigt som belöningen (lön, anseende och karriärmöjligheter) är liten skapar det en stressituation. För att bestämma graden av krav, kontroll, ansträngning och belöning används särskilda frågeformulär. I vår studie undersökte vi sambandet mellan arbetsrelaterad stress beskriven enligt dessa två modeller och förändringar i EKG. Eftersom EKG-förändringar ofta är tecken på hjärtsjukdom skulle ett sådant samband stärka den bevisning som finns att stress i arbetet ökar risken för hjärtkärlsjukdom.

Vi tittade på:

- Hjärtfrekvensen då man tidigare sett att hög och eventuellt låg vilohjärtfrekvens förmodligen kan öka risken för hjärtkärlsjukdom.
- Förmaksflimmer eftersom det ökar risken för stroke.
- Vänstergrenblock, som kan tyda på flera olika hjärtsjukdomar och är en skada på celler i hjärtat som leder den elektriska signal som får hjärtmuskelcellerna att dra ihop sig.

- QTc-intervall. Detta beskriver tidsåtgången för delar av den elektriska aktiviteten i hjärtat. Ett förlängt QTc-intervall ökar risken för hjärtrytmrubbningar som kan leda till hjärtstopp.

Drygt tusen slumpmässigt utvalda personer i Västra Götalandsregionen ingick i studien. Uppgifter om stress i arbetet och EKG samlades in år 2001-2004 som en del i ett annat forskningsprojekt. Dessa uppgifter hämtades ur en databas för att användas i vår studie.

Risken för förlängt QTc-intervall var lika hög hos de med som utan arbetsrelaterad stress och antalet fall av förmaksflimmer och vänstergrenblock var så få att man inte kunde uttala sig om risken var ökad eller minskad i grupperna med arbetsrelaterad stress. Hög vilohjärtfrekvens (över 73 slag/minut) var mindre vanligt bland de som upplevde höga krav och låg kontroll i arbetet jämfört med de som inte gjorde det. Detsamma gällde troligtvis låg vilohjärtfrekvens (under 50 slag/minut) men det kunde inte sägas helt säkert utifrån våra data. Eftersom hög och låg vilohjärtfrekvens tidigare sammanlänkats med en ökad risk för hjärtkärlsjukdom skulle detta kunna tolkas som att arbetsrelaterad stress är kopplad till en minskad risk för hjärtkärlsjukdom. Detta motsäger dock majoriteten av tidigare forskning och våra resultat saknar dessutom stöd från andra studier. Man bör därför inte dra en sådan slutsats innan fler studier bekräftat våra fynd.

Sammanfattningsvis kunde studien alltså inte styrka att arbetsrelaterad stress leder till en ökad risk för hjärtkärlsjukdom. Mer forskning behövs dock inom detta viktiga område i framtiden. Stress i arbetet är ett utbrett problem i dagens samhälle. Om det verkligen föreligger ett samband med hjärtkärlsjukdom skulle förebyggande åtgärder på arbetsplatser kunna förbättra hälsan för ett stort antal människor. Innan sådana åtgärder kan vidtas behöver dock sambandet vara väl underbyggt.

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Tables and appendices

Table 1 General characteristics of the original cohort before exclusions

	Total	Men	Women
N (%)[1]	3614	1704 (47.1)	1910 (52.9)
Mean age (SD)	51.4 (13.1)	51.6 (12.9)	51.2 (13.3)
Valid ECG	3227	1521	1706
Mean heart frequency (SD)	61.9 (10.1)	60.8 (10.6)	62.9 (9.5)
Mean QTc (ms) (SD)	415.2 (23.0)	411.0 (22.9)	418.9 (22.4)
Atrial fibrillation, n	30	23	7
LBBB, n	26	13	13

[1]Row percentage

Table 2 General characteristics of the job strain sample

	All	Job strain	No job strain
N (%)[1]			
Men	752	170 (22.6)	582 (77.4)
Women	800	286 (35.8)	514 (64.2)
Total	1552[a]	456 (29.4)	1096 (70.6)
Mean age (SD)			
Men	46.6 (10.4)	45.0 (10.4)	47.0 (10.3)
Women	45.4 (10.2)	45.6 (10.0)	45.3 (10.4)
Total	46.0 (10.3)	45.4 (10.1)	46.2 (10.4)
Mean heart frequency (SD)			
Men	59.4 (10.0)	59.9 (9.0)	59.3 (10.3)
Women	62.4 (9.5)	62.6 (8.9)	62.3 (9.9)
Total	61.0 (9.9)	61.6 (9.0)	60.7 (10.2)
Mean QTc (ms) (SD)			
Men	407.9 (20.4)	406.6 (20.5)	408.3 (20.4)
Women	416.9 (21.5)	415.7 (22.6)	417.6 (20.8)
Total	412.5 (21.5)	412.3 (22.2)	412.6 (21.1)
Atrial fibrillation, n			
Men	3	1	2
Women	2	0	2
Total	5	1	4
LBBB, n			
Men	3	1	2
Women	3	2	1
Total	6	3	3
Current smoker, (%)[1]			
Men	95	29 (30.5)	66 (69.5)
Women	165	59 (35.8)	106 (64.2)
Total	260	88 (33.8)	172 (66.2)

[1]Row percentage
[a]Valid cases for all categories were 1552, except for "current smoker" where valid cases = 1538

Table 3 General characteristics of the effort-reward sample

	All	Effort-reward ratio > 1	Effort-reward ratio ≤ 1
N (%)[1]			
Men	544	42 (7.7)	502 (92.3)
Women	550	49 (8.9)	501 (91.1)
Total	1094[a]	91 (8.3)	1003 (91.7)
Mean age (SD)			
Men	46.9 (10.2)	45.3 (10.6)	47.0 (10.2)
Women	45.6 (10.1)	45.8 (9.5)	45.5 (10.1)
Total	46.2 (10.2)	45.6 (10.0)	46.3 (10.2)
Mean heart frequency (SD)			
Men	59.6 (10.0)	60.6 (9.7)	59.5 (10.1)
Women	62.7 (9.5)	61.7 (9.1)	62.8 (9.5)
Total	61.2 (9.9)	61.2 (9.3)	61.2 (9.9)
Mean QTc (ms) (SD)			
Men	408.5 (20.9)	405.6 (17.9)	408.7 (21.1)
Women	416.5 (20.8)	414.1 (23.6)	416.7 (20.5)
Total	412.5 (21.2)	410.2 (21.5)	412.7 (21.2)
Atrial fibrillation, n			
Men	2	0	2
Women	2	0	2
Total	4	0	4
LBBB, n			
Men	3	0	3
Women	3	0	3
Total	6	0	6
Current smoker, (%)[1]			
Men	68	9 (13.2)	59 (86.8)
Women	103	8 (7.8)	95 (92.2)
Total	171	17 (9.9)	154 (90.1)

[1]Row percentage
[a]Valid cases for all categories are 1094, except for "current smoker" where valid cases = 1082

Table 4 Linear regression between job strain and effort-reward imbalance and heart frequency

	Job strain (95 % CI)	p-value	ER imbalance (95 % CI)	p-value
Model 1				
-Regression coefficient, total	0.86 (-0.22;1.94)	0.12	0.07 (-2.05;2.19)	0.95
-Regression coefficient, men	0.64 (-1.08;2.35)	0.47	1.17 (-2.00;4.33)	0.47
-Regression coefficient, women	0.22 (-1.16;1.60)	0.75	-1.12 (-3.90;1.66)	0.43
Model 2				
-Regression coefficient, total	0.35 (-0.73;1.43)	0.53	-0.07 (-2.02;2.19)	0.95
-Regression coefficient, men	0.58 (-1.15;2.30)	0.51	1.14 (-2.02;4.29)	0.48
-Regression coefficient, women	0.15 (-1.70;1.56)	0.93	-1.40 (-4.19;1.39)	0.32

Model 1: Unadjusted. Model 2: Adjustments were made for gender, age and current smoking in the non-stratified models and for age and current smoking in the models stratified for gender. Each model is presented without intercepts. Regression coefficient = 0 assumed.

Table 5 Linear regression between job strain and effort-reward imbalance and QTc

	Job strain (95 % CI)	p-value	ER imbalance (95 % CI)	p-value
Model 1				
-Regression coefficient, total	-0.28 (-2.72;1.97)	0.75	-2.54 (-7.09;2.02)	0.28
-Regression coefficient, men	-1.66 (-5.16;1.84)	0.35	-3.10 (-9.69;3.49)	0.36
-Regression coefficient, women	-1.98 (-5.08;1.13)	0.21	-2.63 (-8.75;3.49)	0.40
Model 2				
-Regression coefficient, total	-1.57 (-3.88;0.74)	0.18	-2.54 (-7.05;1.96)	0.27
-Regression coefficient, men	-0.94 (-4.45;2.57)	0.60	-1.92 (-8.53;4.69)	0.57
-Regression coefficient, women	-1.86 (-4.96;1.24)	0.24	-2.89 (-9.06;3.29)	0.36

Model 1: Unadjusted. Model 2: Adjustments were made for gender, age and current smoking in the non-stratified models and for age and current smoking in the models stratified for gender. Each model is presented without intercepts. Regression coefficient = 0 assumed.

Table 6 Correlation between the ER ratio and heart frequency and QTc

	Pearson correlation (R)	R^2
Heart frequency	-0.04	0.002
QTc	-0.02	0.0004

Adjustments were made for gender, age and current smoking.

Table 7 Distributions of heart frequencies in the job strain sample

	Job strain		No job strain		Prevalence OR[3]	P-value[4]
	N	Column %	N	Column %	(95 % CI)	
HF ≥ 90^{th} percentile[1]	39	8.6	122	11.1		
HF < 90^{th} percentile	417	91.4	974	88.9	0.75 (0.51;1.09)	0.13
HF ≤ 10^{th} percentile[2]	35	7.7	127	11.6		
HF > 10^{th} percentile	421	92.3	969	88.4	**0.63 (0.43;0.94)**	**0.02**

[1] 90^{th} percentile = 74 bpm [2] 10^{th} percentile = 49 bpm

$$^{3}POR = \frac{Odds\ for\ being\ exposed\ to\ job\ strain\ if\ HF \geq 90th\ or\ HF \leq 10th\ percentile\ respectively}{Odds\ for\ not\ being\ exposed\ to\ job\ strain\ if\ HF \geq 90th\ or\ HF \leq 10th\ percentile\ respectively}$$

[4]From chi-square tests, no difference in prevalence between groups assumed.

Table 8 Distributions of heart frequencies in the effort-reward sample

	ER ratio > 1		ER ratio ≤ 1		Prevalence OR (95 % CI)	P-value[5]
	N	Column %	N	Column %		
HF ≥ 90^{th} percentile[1]	8	8.8	109	10.9		
HF < 90^{th} percentile	83	91.2	894	89.1	0.79 (0.37;1.68)	0.54
HF ≤ 10^{th} percentile[3]	7	7.7	107	10.7		
HF > 10^{th} percentile	84	92.3	896	89.3	0.70 (0.32;1.55)	0.37

[1] 90^{th} percentile = 74 bpm [2] 10^{th} percentile = 49 bpm
[3]From chi-square tests, no difference in prevalence between groups assumed.

Table 9 Multiple logistic regression for job strain and distributions of heart frequencies

	Estimate	95 % CI	P-value
HF ≥ 90th percentile			
-Odds ratio[1], total	**0.65**	**0.44;0.96**	**0.03**
-Odds ratio, men	0.65	0.33;1.28	0.21
-Odds ratio, women	0.63	0.39;1.02	0.06
HF ≤ 10th percentile			
-Odds ratio[1], total	0.73	0.49;1.09	0.13
-Odds ratio, men	0.72	0.42;1.24	0.24
-Odds ratio, women	0.71	0.39;1.29	0.25

Adjustments were made for gender, age and current smoking in the non-stratified models and for age and current smoking in the models stratified for gender. The age-variable was divided into five categories: age < 30 years, age 30-39 years, age 40-49 years, age 50-59 years and age ≥ 60 years, where the lowest category was used as reference. Each model is presented without intercepts.

[1] Prevalence odds ratio estimated as e^{β} where β is the regression parameter for job strain. $e^{\beta} = 1$ assumed.

Table 10 Prolonged and normal QTc in the job strain sample

	Job strain		No job strain		Prevalence OR[3] (95 % CI)	P-value[4]
	N	**Column %**	**N**	**Column %**		
Prolonged QTc[1], men	6	3.5	18	3.1	1.15 (0.45;2.94)	0.78
Normal QTc, men	164	96.5	564	96.9		
Prolonged QTc[2], women	8	2.8	19	3.7	0.75 (0.32;1.74)	0.50
Normal QTc, women	278	97.2	495	96.3		
Prolonged QTc, total	14	3.1	37	3.4	0.91 (0.49;1.69)	0.76
Normal QTc, total	442	96.9	1059	96.6		

[1] QTc > 450 ms [2] QTc > 460 ms [3] $POR = \frac{Odds\ for\ being\ exposed\ to\ job\ strain\ if\ prolonged\ QTc}{Odds\ for\ being\ exposed\ to\ job\ strain\ if\ normal\ QTc}$

[4] From chi-square tests, no difference in prevalence between groups assumed.

Table 11 Any ECG-changes in the job strain sample

	Job strain		No job strain		Prevalence OR (95 % CI)	P-value[2]
	N	**Column %**	**N**	**Column %**		
Change in ECG[1], men	8	4.7	20	3.4	1.39 (0.60;3.21)	0.44
Normal ECG, men	162	95.3	562	96.6		
Change in ECG[1], women	10	3.5	22	4.3	0.81 (0.38;1.74)	0.59
Normal ECG, women	276	96.5	492	95.7		
Change in ECG[1], total	18	3.9	42	3.8	1.03 (0.59;1.81)	0.92
Normal ECG, total	438	96.1	1054	96.2		

[1] Prolonged QTc, LBBB or atrial fibrillation

[2] From chi-square tests, no difference in prevalence between groups assumed.

Questionnaire for job strain

Demands

	Aldrig	Sällan	Ibland	Ofta	Nästan jämt
04. Hur ofta under det senaste året har det varit extra mycket att göra på Ditt arbete?	☐	☐	☐	☐	☐
05. Hur ofta under det senaste året har det varit en påfallande ökning av Din arbetsbelastning?	☐	☐	☐	☐	☐
06. Hur ofta kräver Ditt arbete en ökad koncentrationsförmåga	☐	☐	☐	☐	☐

Control

12. Har Du möjlighet att bestämma över Din/Dina:					
- Arbetsuppgifter	☐	☐	☐	☐	☐
- Planering av arbetet	☐	☐	☐	☐	☐
- Arbetstider	☐	☐	☐	☐	☐

Questionnaire for effort-reward

B DITT ARBETE *(forts)*

Följande frågor gäller endast Dig som har ett arbete.

Frågorna gäller förhållanden i Ditt arbete. Vi ber Dig ange om Du håller med påståendet eller inte genom att sätta ett kryss i "Nej " eller "Ja" rutan.

Om den svarsruta Du väljer inte har en efterföljande pil, besvara inte följdfrågan, utan gå vidare till nästa påstående.

Om den svarsruta Du väljer har en efterföljande pil, besvara då följdfrågan, om i vilken grad Du upplever förhållandet som en belastning, genom att ringa in den siffra som bäst svarar mot Din bedömning.

		Ingen belastning alls	En mindre belastning	En belastning	En stor belastning
13. Jag arbetar ofta under tidspress på grund av den höga arbetsbördan.	Nej ☐				
	Ja ☐ →	1	2	3	4
14. Jag blir ofta avbruten i mitt arbete.	Nej ☐				
	Ja ☐ →	1	2	3	4
15. Jag har ett stort ansvar i mitt arbete.	Nej ☐				
	Ja ☐ →	1	2	3	4
16. Jag är ofta tvungen att arbeta övertid.	Nej ☐				
	Ja ☐ →	1	2	3	4
17. Mitt arbete är fysiskt påfrestande.	Nej ☐				
	Ja ☐ →	1	2	3	4
18. Jag har fått allt mer att göra på arbetet under de senaste åren.	Nej ☐				
	Ja ☐ →	1	2	3	4
19. Tycker Du att Du får det erkännande av Dina arbetskamrater som Du förtjänar?	Nej ☐ →	1	2	3	4
	Ja ☐				
20. Tycker Du att Du får det erkännande av Dina överordnande som Du förtjänar?	Nej ☐ →	1	2	3	4
	Ja ☐				
21. Får Du det stöd Du behöver i svåra situationer?	Nej ☐ →	1	2	3	4
	Ja ☐				
22. Blir Du orättvist behandlad i Ditt arbete?	Nej ☐				
	Ja ☐ →	1	2	3	4
23. Har Du dåliga möjligheter till avancering inom Ditt område?	Nej ☐				
	Ja ☐ →	1	2	3	4
24. Upplever Du för närvarande eller förväntar Du Dig en negativ förändring i Din arbets-situation?	Nej ☐				
	Ja ☐ →	1	2	3	4
25. Är Du rädd att förlora arbetet?	Nej ☐				
	Ja ☐ →	1	2	3	4
26. Anser Du att Du har ett arbete som rimligen motsvarar Din utbildning?	Nej ☐ →	1	2	3	4
	Ja ☐				
27. Med tanke på allt Du har presterat, tycker Du då att Du har en rimlig lön?	Nej ☐ →	1	2	3	4
	Ja ☐				
28. Med tanke på allt Du har presterat och uträttat, tycker Du då att Du får erkännande och den respekt Du förtjänar?	Nej ☐	1	2	3	4
	Ja ☐				
29. Med tanke på allt Du har presterat och uträttat, tycker Du då att Du har fått möjlighet till personligt avancemang i Ditt yrkesliv?	Nej ☐ →	1	2	3	4
	Ja ☐				