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CARDIORADIOLOGIA

Effect of an oral anxiolytic medication and heart rate variability on image quality of 64-slice MDCT coronary angiography

Effetti della somministrazione di ansiolitici per via orale e della variabilità della frequenza cardiaca sulla qualità delle immagini in angiografia coronarica mediante TC 64 strati (MDCT-CA)

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Abstract
Purpose. The aim of the study was to investigate the relationship between image quality in 64-slice multidetector computed tomography (MDCT) and patients' preimaging anxiety status and heart rate variability (HRV), and to evaluate the efficacy of an orally administered anxiolytic medication on HRV and image quality.
Materials and methods. Sixty patients [14 women, 46 men; mean age 52.53±10.55 (SD), range 33–78 years] were studied. Anxiety levels were assessed with the State-Trait Anxiety Inventory 60 min before the procedure. The participating patients were randomly assigned to one of the two study groups: a control group (no medication administered for anxiety reduction) and an anxiolytic medication group, with 30 patients in each group. The presence of motion artefacts and image quality for each coronary artery segment were evaluated using a four-point grading system. To estimate HRV, the duration of each heartbeat during MDCT data acquisition was measured in each patient.
Results. A moderate correlation was found between HRV during MDCT scanning and the mean image quality for all coronary segments (r=0.47, p<0.01). There was an association between HRV and state anxiety scores in all cases (r=0.370, p<0.01). HRV in the patients who received alprazolam was statistically significantly lower than in controls (p<0.05). The average image quality in patients who used alprazolam was also statistically significantly higher than in controls (p<0.05).
Conclusions. The most important finding in our study is

Riassunto
Obiettivo. *Valutare la relazione tra la qualità delle immagini in TC multidetettore a 64 strati (MDCT), lo stato d'ansia dei pazienti prima dell'esame TC e la variabilità della frequenza cardiaca (HRV); valutare l'efficacia della somministrazione per via orale di ansiolitici sulla variabilità della frequenza cardiaca (HRV) e sulla qualità delle immagini.*
Materiali e metodi. *Sono stati studiati 60 pazienti [14 donne, 46 uomini;età media 52,53±10,55 (DS), intervallo 33–78 anni]. Il livello d'ansia è stato stimato a monte della procedura con l'ausilio della forma Y dello State-Trait Anxiety Inventory 60 (STAI-Y). I pazienti che hanno partecipato allo studio sono stati casualmente assegnati ad uno dei due gruppi di studio: il gruppo di controllo (ai quali non veniva somministrato ansiolitico per ridurre lo stato d'ansia) ed il gruppo dei pazienti trattati con ansiolitici, quest'ultimo composto da 30 pazienti. La presenza di artefatti da movimento e la qualità delle immagini per ciascun segmento coronarico studiato, sono state valutate utilizzando un sistema di classificazione a 4 punti. La stima della variabilità della frequenza cardiaca (HRV) e la durata di ciascun battito cardiaco durante l'acquisizione dei dati in MDCT sono stati misurati in ogni paziente.*
Risultati. *È stata riscontrata una moderata correlazione tra la variabilità della frequenza cardiaca (HRV) durante l'acquisizione delle immagini MDCT e la media della qualità dell'immagine per tutti i segmenti coronarici studiati (r=0,47, p<0,01). Vi era una concordanza tra la variabilità della frequenza cardiaca (HRV) ed il livello d'ansia in tutti i*

that oral premedication to reduce anxiety is also effective in decreasing HRV and improves image quality. Therefore, we suggest that using alprazolam in addition to a β-blocker may improve image quality in patients undergoing MDCT coronary angiography (MDCT-CA). Anxiolytic usage may improve image quality by lowering the HRV in selected cases where administration of a β-blocker is contraindicated. We also suggest that further studies in larger series are required to validate this finding.

Keywords Multidetector computed tomography · Coronary angiography · Heart rate · Benzodiazepines · Premedication

casi (r=0,370, p<0,01). La variabilità della frequenza cardiaca (HRV) nei pazienti trattati con alprazolam era significativamente più bassa che nei controlli (p<0,05). Anche la qualità delle immagini nei pazienti trattati con alprazolam era significativamente più elevata che nei controlli (p<0,05).

Conclusioni. *Il riscontro del nostro studio è che la premedicazione con ansiolitici per via orale riduce lo stato d'ansia ed è efficace anche nel ridurre la variabilità della frequenza cardiaca (HRV) e nel migliorare la qualità delle immagini. Pertanto, suggeriamo che l'utilizzo dell'alprazolam in combinazione con gli β-litici potrebbe migliorare la qualità delle immagini nei pazienti sottoposti ad angiografia coronarica mediante TC multidetettore (MDCT-CA). L'utilizzo degli ansiolitici potrebbe migliorare la qualità delle immagini diminuendo la variabilità della frequenza cardiaca (HRV) in casi selezionati dove è controindicata la somministrazione degli β-litici. Per poter validare questi risultati sono necessari ulteriori studi su casistiche più ampie.*

Parole chiave *Tomografia computerizzata multidetettore · Angiografia Coronarica · Frequenza cardiaca · Benzodiazepine · Premedicazione*

Introduction

The main limitation to the use of multidetector row computed tomography (MDCT) in coronary angiography (CA) is temporal resolution [1–3]. With the introduction of 64-detector MDCT, the problem of temporal resolution has been substantially resolved, but image quality remains poor in patients with high heart rates (HR) [3–5]. Leschka et al. recently investigated the effect of heart rate variability (HRV) in addition to HR on image quality in their study performed with 64-detector MDCT [6, 7]. They reported that reduced HRV as well as HR during MDCT imaging reduces motion artefacts [6]. In another study in which they compared MDCT-CA and invasive CA, they reported that a low HRV increases the diagnostic accuracy of 64-detector MDCT-CA [7]. Matt et al., from the same institute (Institute of Diagnostic Radiology, University Hospital Zurich), reported that HR that are both high and variable deteriorate image quality in dual-source MDCT, but the quality remains adequate for diagnosis [4]. Currently, β-blocker administration for premedication is used as the standard procedure to reduce HR in CA performed by MDCT with low detector counts, including 64 detectors [8–11]. It is reported that β-blocker administration increases image quality by reducing the HR or, additionally, the HRV [6, 7].

As in many medical procedures, patients can be stressed before undergoing MDCT-CA, and the complication rates increase due to impaired patient compliance [12, 13]. For this reason, anxiolytic usage for premedication in invasive CA has been reported [14, 15]. Additionally, the radiology literature reports that orally and intravenously administered anxiolytic premedications prior to interventional radiology procedures increase patient compliance [16, 17]. In addition to the stress originating from MDCT imaging, the potentially bad results of the examination can produce high anxiety, especially in patients with coronary artery disease (CAD) for whom the outcome is of vital importance.

We performed a literature review and could find no study evaluating the relationship between the use of anxiolytic premedication before MDCT-CA, patients' anxiety status and HRV/image quality. Therefore, the purposes of this study were to investigate the relationship between image quality in 64-detector MDCT and preimaging anxiety status and HRV and to evaluate the efficacy of an orally administered anxiolytic medication on HRV and image quality.

Materials and methods

Patient population

A total of 91 patients were referred for MDCT-CA due to

Table 1 Demographic and clinical data of patients with and without alprazolam medication

Tabella 1 *Dati demografici e clinici dei pazienti trattati e non trattati con Alprazolam*

Characteristics	Patients receiving alprazolam medication	Patients not receiving alprazolam medication (control group)	Total	*p* value
No. of patients	30 3	0	60	
Age (years)	50.43±10.65	54.65±10.37	52.53±10.55	0.124* ($p>0.05$)
Male-to-female ratio	22/8	24/6	46/14	0.542** ($p>0.05$)
Body mass index (kg/m^2)	28.1±3.7	27.8±2.9	28±3.6	0.659* ($p>0.05$)
Average heart rate (beats/min)	58.6±7.3	62.5±9.7	60.7±9.5	0.080* ($p>0.05$)
Heart rate variability (beats/min)[a]	2.4±1.4	4.5±3.0	3.4±2.6 (2.83)	0.001*** ($p<0.01$)
Family history	14 (47%)	12 (%40)	26 (43%)	0.602** ($p>0.05$)
Hypertension	11 (37%)	10 (33%)	21 (35%)	0.787** ($p>0.05$)
Hyperlipidaemia	14 (47%)	15 (50%)	29 (48%)	0.796** ($p>0.05$)
Diabetes mellitus	8 (27%)	10 (33%)	18 (30%)	0.573** ($p>0.05$)
Smoking	8 (27%)	11 (37%)	19 (32%)	0.405** ($p>0.05$)
No. of patients using β-receptor antagonist	10 (33%)	8 (27%)	18 (30%)	0.573** ($p>0.05$)
No. of patients using calcium-channel blockers	4 (13%)	1 (3%)	5 (8.3%)	0.35*** ($p>0.05$)
Additional β-blocker medication in MDCT	12 (40%)	10 (33%)	22 (37%)	0.592** ($p>0.05$)

Values are number (%) or mean±standard deviation (SD)
*Student's *t* test, ** chi-square test, ***Fisher's exact test
[a]Heart rate variability (HRV) was calculated as the SD of HR during scanning

clinically suspected CAD between April 2009 and August 2009 [18]. Evaluated by an experienced cardiologist, the patients had a low/intermediate risk for CAD. Sixty patients [14 women, 46 men; mean age 52.53±10.55 standard deviation (SD), range 33–78 years] were included. Twenty patients in whom MDCT-CA was not performed due to the following clinical conditions were excluded: absolute arrhythmia (e.g. atrial fibrillation) (n = 8), renal dysfunction (serum creatinine>1.2 mmol/l) (n=7), a history of allergic reaction to iodine-containing contrast media (n=4) and pregnancy (n=1). We also excluded 11 patients who had a history of anxiety reduction medication or coronary artery bypass surgery, although they were examined with MDCT. At the time of CT, 23 (38.3%) patients were taking β-receptor antagonists (n=18) and calcium-channel blockers (n=5). There were no statistically significant differences in patients' ages, body mass index (BMI), gender, average HR, risk factors or chronic consumption of cardiovascular drugs between the two subgroups. The demographic data, risk factors and chronic consumption of cardiovascular drugs for the two subgroups are summarised in Table 1. The study was approved by the local institutional review board, and informed consent was obtained from each patient.

Anxiety assessment method

All patients' anxiety levels were assessed with the State-Trait Anxiety Inventory (STAI) 60 min before the procedure by an investigator (PG) [19]. State anxiety refers to the temporary anxiety condition of an individual in a specific situation and a specific moment. In contrast, trait anxiety refers to how an individual feels, independent of the situation, and is a more general and longstanding condition [19]. The STAI is a 40-item self-reported questionnaire (20 state anxiety statements and 20 trait anxiety statements). Responses to each of the 40 questions are given according to a scoring scale from 1 (not at all) to 4 (very much so). Each anxiety score can range between 20 and 80. The test has been validated in various patient groups and college students [19].

The participating patients were randomly assigned to one of the two study groups: a control group (no medication administered for anxiety reduction) and an anxiolytic medication group. Patients were consecutively registered to the study list with a unique number. patients with an odd study registration number were assigned to the anxiolytic medication group, and those with an even number were assigned to the control group. Alprazolam 0.5 mg tablets (Xanax; Pharmacia & Upjohn, Peapack, NJ, USA) was administered orally 30–45 min prior to MDCT to the anxiolytic medication group. Thus, we had two separate groups with 30 patients in each. Age and gender distribution within the groups was as follows: the anxiolytic medication group (8 women, 22 men; mean age 50.43±10.65 (SD) years, range 33–70 years) and the control group (6 women, 24 men; mean age 54.65±10.37 (SD) years, range 35–78 years].

MDCT examination technique

Data were acquired using a 64-detector-row spiral CT scanner (Aquilion 64 Slice, Toshiba Medical Systems, Tokyo, Japan). The scan parameters were 64×0.5-mm detector collimation, pitch 0.2–0.45 (depending on HR), rotation time 400 ms, tube voltage 120 kV, current 600–900 effective mAs. Electrocardiogram (ECG)-dependent tube current modulation was applied in regular HRs <65 bpm. Scan direction was craniocaudal during a single midinspiratory breath-hold.

A bolus of 80 ml iodine contrast agent iobitridol (Xenetix 350, 350mg/ml; Guerbet, France) was administered intravenously into an antecubital vein at a flow rate of 5–6 ml/s using a dual-head power injector, followed by 50-ml saline chaser (5 ml/s). The scan was started automatically by applying the "sure start" technique (ascending aorta, threshold 160 HU). The scanning range covered the entire heart from the level of the tracheal bifurcation to the diaphragm. A β-blocker was given intravenously before the MDCT scan if the HR was>70 beats per min (5–15 ml metoprolol), regardless of grouping. No complication was encountered during the procedures. None of the patients reported any discomfort due to the CT protocol or the use of contrast media or alprazolam medication.

MDCT image reconstruction and analysis

During the scan, ECG was recorded simultaneously. The retrospective reconstructions were done in all cardiac phases, with 50-ms intervals (from 20% to 80% of the R-R interval). Images were reconstructed with a section thickness of 0.5 mm, a reconstruction increment of 0.3mm, image matrix 512×512 and FOV of 180–240 mm. Data were transferred to software Vitrea 2 workstation (Vital Images Inc., Plymouth, MN, USA), and images were reconstructed with multiple postprocessing methods.

MDCT images were evaluated and classified by two radiologists (RC, NT) experienced in cardiovascular radiology. When the two radiologists had different opinions, the final decision was obtained by consensus. Segmental evaluation of the coronary arteries was performed according to the American Heart Association's (AHA) 15-segment classification [20]: right coronary artery (RCA) 1–4; left main (LM) and left anterior descending artery (LAD) 5–10; left circumflex artery (LCX) 11–15. All segments were included in the assessment. Transverse source images, multiplanar reformations, curved multiplanar reformations, and maximum intensity projection images were used to evaluate coronary segments. The presence of motion artefacts and image quality for each coronary artery segment were evaluated in a semiqualitative fashion using a four-point grading system, where a score of 1 indicates no motion artefacts, clear delineation of the segment; a score of 2 indicates good, with minor artefacts, mild blurring of the segment; a score of 3 indicates adequate, with moderate artefacts, moderate blurring without structure discontinuity; and a score of 4 indicates nonevaluable, with doubling or discontinuity in the course of the segment preventing evaluation or vessel structures not differentiable.

From the recorded ECG information, the HR in each cardiac cycle was noted by another author (SY), who did not participate in image assessment. To estimate HRV, the duration of each heartbeat during CT data acquisition was measured in each patient. From this set of measurements, the variability in HR during scanning was calculated as the SD from the average HR [6].

Statistical analysis

The statistical software NCSS 2007 & PASS 2008 (UT, USA) was used for statistical analyses. In analysing the study data, Student's *t* test was used to evaluate parameters with a normal distribution between groups for quantitative data, besides descriptive statistical methods (mean, SD, frequency); and the relationships between parameters were tested by Pearson's correlation analysis and linear regression analysis. Interobserver agreement was evaluated by Cohen's kappa analysis. Chi-square test and Fisher's exact test were used to analyse categorical data in the two groups. Results were evaluated at 95% confidence interval (CI) at the significance level $p<0.05$.

Results

The average HR was 60.7±9.6 (range 44–94 beats per min). A total of 17 cases (28%) had stable heartbeat, and there was only one to two beats difference during the whole MDCT imaging [6]. The heartbeat was completely irregular in ten cases (17%) and changed continuously in subsequent cardiac cycles. Heart rate showed mild/moderate variability within a range below and above baseline values in the other cases (65%).

Image quality of the coronary arteries

A total of 881 coronary artery segments were evaluated. Nineteen segments could not be evaluated due to a very low calibre (<1.5 mm) or anatomical variations. The best reconstruction interval was used to evaluate image quality. Percentages for the coronary segment scores observed were 65% (575/881) for score 1, 26% (226/881) for score 2 and 8% (69/881) for score 3. There were only 11 coronary segments (1%) with a score of 4 (Fig. 1). For image quality score, interobserver agreement was good (κ=0.76). The

Fig. 1a-d Curved multiplanar reformations of 64-slice multidetector computed tomography (MDCT) images of right coronary artery (RCA) in patients with four different semiquantitative four-point image-quality scores. Score 1: no motion artefacts, clear delineation of the segment; score 2: good, with minor artefacts, mild blurring of the segment; score 3: adequate, with moderate artefacts, moderate blurring without structure discontinuity, score 4: nonevaluable, doubling or discontinuity in the course of the segment preventing evaluation, or vessel structures not differentiable.

Fig. 1 a-d *Immagini di ricostruzione MPR-curved, ottenute con TC multidetettore a 64 strati, dell'arteria coronaria destra (RCA) in Pazienti con quattro differenti punteggi semiquantitativi di qualità dell'immagine, calcolati in base a quattro punti. Punteggio 1: assenza di artefatti da movimento, chiara delineazione del segmento; Punteggio 2: buono, con un minor numero di artefatti, e medio "offuscamento" del segmento; Punteggio 3: adeguato, con un moderato numero di artefatti, e moderato "offuscamento" senza discontinuità della struttura; Punteggio 4: non valutabile, sdoppiamento o discontinuità nel percorso del segmento che non ne permette la valutazione, o strutture vascolari non differenziabili.*

mean image quality scores for coronary segments in all patients were as follows: RCA (1.50±0.39); LM (1.31±0.47); LAD (1.35±0.29) and LCX (1.39±0.34). Image quality scores are summarised in Table 2.

Effect of heart rate variability on image quality

A correlation was found between HRV during MDCT scanning and the mean image quality of all coronary segments

Table 2 Image quality scores of coronary arteries for all patients

Tabella 2 *Punteggio della qualità di immagine delle arterie coronarie per ciascun Paziente*

Characteristics	Patients receiving alprazolam medication	Patients not receiving alprazolam medication (control group)	Total	*p* value
Mean image quality scores for coronary artery				
All coronary arteries (median)	1.31±0.31 (1.16)	1.48±0.35 (1.35)	1.39±0.34	0.008** ($p<0.01$)
RCA (median)	1.43±0.39 (1.25)	1.58±0.38 (1.50)	1.50±0.39	0.018** ($p<0.05$)
LM	0.17±0.37	1.47±0.51	1.31±0.47	0.012* ($p<0.05$)
LAD	1.31±0.24	1.40±0.33	1.35±0.29	0.255** ($p>0.05$)
LCX	1.32±0.27	1.47±0.38	1.39±0.34	0.036* ($p<0.05$)
Percentage of patients with score (%)[a]				
Score 1	71 (315/444)	61 (266/437)	581	
Score 2	23 (103/444)	27 (119/437)	222	
Score 3	5 (21/444)	11 (47/437)	68	
Score 4	1 (5/444)	1 (5/437)	10	

Unless otherwise specified, data are means±standard deviations (SD)
RCA right coronary artery, *LM* left main, *LAD* left anterior descending, *LCX* left circumflex
*Student's *t* test, **Mann–Whitney *U* test
[a]For each score, the percentage of coronary artery segments with that score is given, with numbers of segments in parentheses. Scores were defined as follows: 1, no motion artefacts; 2, minor artefacts; 3, moderate artefacts; 4, not evaluable

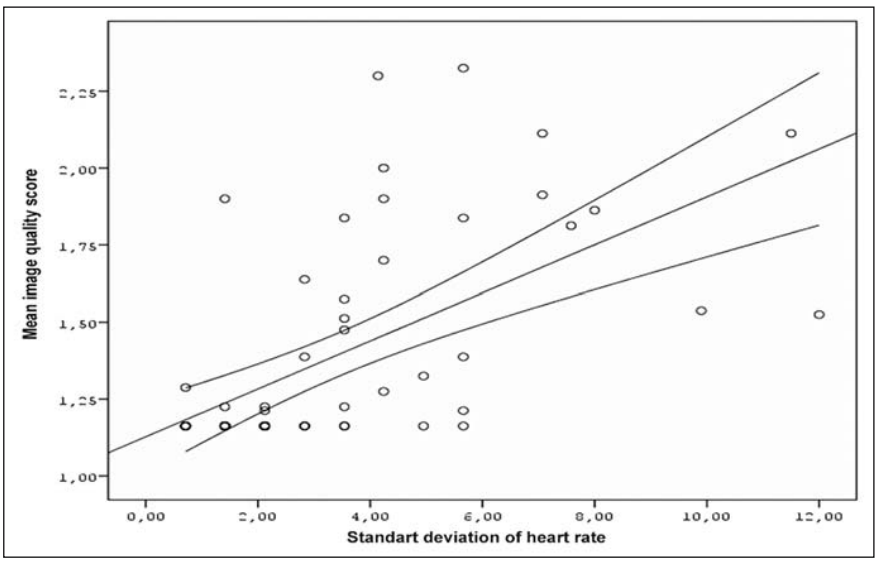

Fig. 2 Relationship between standard deviation of heart rate and mean image quality (Pearson correlation, $r=0.59$; $p<0.001$).

Fig. 2 *Relazione tra deviazione standard della frequenza cardiaca e qualità di immagine media (correlazione secondo Perarson, r=0,59, p<0,001).*

($r=0.47$, $p<0.01$) (Fig. 2). This relationship reached the highest level in RCA ($r=0.46$, $p<0.01$), and the rest were determined to be as those in LAD ($r=0.43$, $p<0.01$), LM ($r=0.40$, $p<0.01$) and LCX ($r=0.40$, $p<0.01$). There was a significant correlation between average HR and mean image quality scores for all coronary segments ($r=0.51$, $p<0.01$).

Effect of anxiety scores and alprazolam medication on heart rate variability and image quality

State anxiety scores of all cases varied between 21 and 49; the mean value was 33.75±7.86. On the other hand, trait anxiety scores varied between 21 and 57, and mean value was 39.56±7.95. There was an association between HRV and state anxiety scores in all cases ($r=0.370$, $p<0.01$). There was no statistically significant relationship between HRV and trait anxiety scores ($r=0.214$, $p>0.05$). Although state anxiety scores of patients who received alprazolam were lower than patients in the control group (32.03±7.57 versus 35.46±7.89, respectively), the difference was not statistically significant ($p>0.05$). No statistically significant difference was noted between the groups with and without alprazolam with regard to trait anxiety scores (39.93±7.79 and 39.20±8.23, respectively) ($p>0.05$).

HRV in patients who used alprazolam was determined to be statistically significantly lower than in controls (2.4 ±1.4 versus 4.5 ±3.0, respectively). The average image quality in patients who received alprazolam was also statistically significantly higher than in controls (1.31 ±0.31 versus 1.48 ±0.35, respectively). Although there was a weak negative association between HRV and state anxiety scores (r=-0.104, p>0.05) and trait anxiety scores (r=-0.315, p>0.05) in patients who received alprazolam, it was not statistically significant. On the other hand, there was a statistically significant positive relationship between HRV and state anxiety scores (r=0.636, p<0.01) and trait anxiety scores (r=0.610, p<0.01) in patients who did not use alprazolam.

Discussion

In bearing with previous studies [4, 6, 7], a correlation was found between HRV and mean image quality of all coronary segments. We detected an association between state anxiety scores and HRV in all cases in our study, which is the first of its kind in the literature. HRV was lower and image quality higher in patients who received alprazolam when compared with the control group.

It has been reported that HRV occurring during MDCT imaging influences image quality [4, 6, 7]. The most specific and largest studies investigating this issue have been performed by Leschka et al. In their study using 64-detector-row MDCT, they reported that HRV is associated with mean image quality of all coronary segments, and in particular, RCA is more heavily affected by HRV [6]. Additionally, they reported that low HRV is associated with a higher diagnostic accuracy of 64-detector-row MDCT-CA [7]. Dual-source MDCT-CA is reported to be sufficient for diagnosis in high HR and HRV, but image quality deteriorates in the case of both high and variable HRs [4]. A very moderate correlation between HRV during MDCT scanning and mean image quality of all coronary segments was found in our study, as well. Image quality of RCA, LAD, LM and LCX deteriorated due to HRV in an order from higher to lower. The main limitation to the use of MDCT-CA has been temporal resolution and cardiac motion. Heart rate can be reduced with β-blockers or calcium-channel blockers [21–23]. β-blocker administration is routinely used to reduce HR during cardiac imaging, including studies with 64-slice MDCT scanners [8–11]. Leschka et al. reported that β-blockers reduce HRV as well as HR and thus increase the image quality. They propose β-blocker usage in the event of increased HRV, even if HR is only slightly high [6, 7].

Patients usually have high anxiety levels prior to radiological and other medical procedures. The increase in sympathetic activity due to this anxiety causes unintentional movement and momentary changes in HR and blood pressure [12]. Anxiolytic usage is reported for premedication in invasive CA to reduce this effect [14, 15]. In our study, there was an association between HRV and the mood (state anxiety scores) of patients before the procedure. In other words, as the anxiety level of the patient increased, HRV increased as well, and image quality deteriorated. However, there was no statistically significant relationship between trait anxiety scores, which reflect how an individual feels independent of the situation and conditions (a more general and longstanding condition), and HRV. Increased anxiety prior to imaging (state anxiety scores) caused an increase in HRV, probably due to elevated sympathetic activity. It is remarkable that trait anxiety scores and HRV do not change. Therefore, we can hypothesise that if we reduce the momentary anxiety in patients prior to MDCT imaging, we can decrease the HRV and avoid deterioration in image quality.

In our literature search, we could not identify any previous study related to anxiety reduction specifically for MDCT-CA. Benzodiazepines are the most commonly used anxiolytic drugs in the radiology department and are considered safe, with minimal respiratory and cardiovascular effects [12]. Alprazolam used in our study is one of the most frequently prescribed benzodiazepines for treating panic disorders [24]. Benzodiazepines act selectively on central g-aminobutyric acid (GABA)-A receptors and enhance response to the GABA inhibitory neurotransmitter. Benzodiazepines inhibit increased noradrenergic activity in the locus ceruleus as well. According to the American Society of Anesthesiologists, the definition for minimal sedation (anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, respiratory and cardiovascular function are thought to be unaffected [12, 25]. Benzodiazepines can be administered both orally and intravenously. The use of intravenous sedation during interventional radiological procedures requires monitoring for respiratory depression. Besides, sedative administration may sometimes require an anaesthesiologist [12, 26]. This may add substantial cost and may not be a feasible option for MDCT-CA. Administration of the oral anxiolytic medication does not require introduction of an intravenous catheter or the presence of a nurse or anaesthesia staff during the procedure. We think that oral alprazolam used in our study is a feasible anxiolytic premedication agent for use prior to MDCT, with its short half-life, rapid effect, inexpensiveness and ease of use when compared with the other benzodiazepines.

We achieved anxiolytic effect with oral alprazolam in our study without affecting respiratory and cardiovascular functions. Nevertheless, it is known that in the presence of other central nervous system depressants, particularly alcohol, they may cause severe respiratory depression, especially in the elderly, children and critically ill patients, as they may result in apnoea [27]. This kind of effect is out of scope of

this particular study, as we excluded such patients initially. On the other hand, HRV decreased and image quality increased significantly in patients receiving alprazolam when compared with the control group. Additionally, whereas HRV increased in parallel with the increase in state anxiety scores in patients not taking alprazolam, there was no such relationship in patients who received alprazolam. We drew the conclusion that alprazolam, used as an anxiolytic, breaks the vicious cycle comprising increased anxiety, increased noradrenergic activity, increased HRV and low image quality.

The first limitation in our study was that we could not examine the individual effects of the β-blocker and alprazolam on image quality. The reasons for this were the relatively small number of patients included in the study, preexisting usage of a β-blocker by some patients or our use of a β-blocker during MDCT to reduce high HR. Additionally, we could not avoid β-blocker use to reduce HR because of our priority for image quality. The second limitation was lack of patient demographic data other than age and gender, such as education, marital status and ethnicity, which may be related with STAI evaluation. In addition, combined placebo administration may play a significant role over patient mood (state anxiety scores). However, as our first aim was to lower the HRV and increase image quality rather than evaluate the effect of alprazolam on mood, we neither used combined placebo administration nor collected the postprocedure state anxiety scores of our patients. This may be a major aim of a further study on this topic.

In conclusion, the most important finding in our study was that orally administered premedication to reduce anxiety reduces HRV as well and improves image quality. Therefore, we suggest that using alprazolam in addition to a β-blocker may improve image quality in patients undergoing cardiac imaging. It may be more effective in patients with a variable HR who are visually thought to be anxious before MDCT imaging. However, further studies should be conducted considering this visual determination. Moreover, anxiolytic usage can improve image quality by lowering HRV in selected patients in whom administration of a β-blocker is contraindicated. We also suggest that further studies with larger series are performed to validate this finding.

Conflict of interest None

References/*Bibliografia*

1. Schoepf UJ, Becker C, Ohnesorge BM, Yucel K (2004) CT of coronary artery disease. Radiology 232:18–37
2. Schoenhagen P, Halliburton SS, Stillman AE et al (2004) Noninvasive imaging of coronary arteries: current and future role of multi-detector row CT. Radiology 232:7–17
3. Oncel D, Oncel G, Tastan A (2007) Effectiveness of dual-source CT coronary angiography for the evaluation of coronary artery disease in patients with atrial fibrillation: initial experience. Radiology 245:703–711
4. Matt D, Scheffel H, Leschka S et al (2007) Dual-source CT coronary angiography: image quality, mean heart rate, and heart rate variability. AJR Am J Roentgenol 189:567–573
5. Wintersperger BJ, Nikolaou K, von Ziegler F et al (2006) Image quality, motion artifacts, and reconstruction timing of 64-slice coronary computed tomography angiography with 0.33-second rotation speed. Invest Radiol 41:436–442
6. Leschka S, Wildermuth S, Boehm T et al (2006) Noninvasive coronary angiography with 64-section CT: effect of average heart rate and heart rate variability on image quality. Radiology 241:378–385
7. Leschka S, Scheffel H, Husmann L et al (2008) Effect of decrease in heart rate variability on the diagnostic accuracy of 64-MDCT coronary angiography. AJR Am J Roentgenol 190:1583–1590
8. Achenbach S, Giesler T, Ropers D et al (2001) Detection of coronary artery stenoses by contrast-enhanced, retrospectively electrocardiographically-gated, multislice spiral computed tomography. Circulation 103:2535–2538
9. Nieman K, Cademartiri F, Lemos PA et al (2002) Reliable noninvasive coronary angiography with fast submillimeter multislice spiral computed tomography. Circulation 106:2051–2054
10. Heuschmid M, Kuettner A, Schroeder S et al (2005) ECG-gated 16-MDCT of the coronary arteries: assessment of image quality and accuracy in detecting stenoses. AJR Am J Roentgenol 184:1413–1419
11. Pugliese F, Mollet NR, Runza G et al (2006) Diagnostic accuracy of non-invasive 64-slice CT coronary angiography in patients with stable angina pectoris. Eur Radiol 16:575–582
12. Patatas K, Koukkoulli A (2009) The use of sedation in the radiology department. Clin Radiol 64:655–663
13. Mueller PR, Biswal S, Halpern EF et al (2000) Interventional radiologic procedures: patient anxiety, perception of pain, understanding of procedure, and satisfaction with medication-a prospective study. Radiology 215:684–688
14. Woodhead J, Harding SA, Simmonds M et al (2007) Premedication for cardiac catheterization and percutaneous coronary intervention: does it increase vascular access site complications? J Cardiovasc Nurs 22:466–471

15. Beddoes L, Botti M, Duke MM (2008) Patients' experiences of cardiology procedures using minimal conscious sedation. Heart Lung 37:196–204
16. Bugbee ME, Wellisch DK, Arnott IM et al (2005) Breast core-needle biopsy: clinical trial of relaxation technique versus medication versus no intervention for anxiety reduction. Radiology 234:73–78
17. van Vlymen JM, Sa Rego MM, White PF (1999) Benzodiazepine premedication: can it improve outcome in patients undergoing breast biopsy procedures? Anesthesiology 90:740–747
18. Hendel RC, Patel MR, Kramer CM et al (2006) ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging. J Am Coll Cardiol 48:1475–1497
19. Spielberger C, Gorsuch R, Lushene R. State-Trait Anxiety Inventory manual (STAI) (1970) Palo Alto, Calif: Consulting Psychologists.
20. Austen WG, Edwards JE, Frye RL et al (1975) A reporting system on patients evaluated for coronary artery disease: report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation 51:5–40
21. Giesler T, Baum U, Ropers D et al (2002) Noninvasive visualization of coronary arteries using contrast-enhanced multidetector CT: influence of heart rate on image quality and stenosis detection. AJR Am J Roentgenol 179:911–916
22. Pannu HK, Alvarez W Jr, Fishman EK (2006) ,-blockers for cardiac CT: a primer for the radiologist. AJR 186[suppl]:S341–S345
23. Dougherty AH, Jackman WM, Naccarelli GV, Friday KJ, Dias VC (1992) Acute conversion of paroxysmal supraventricular tachycardia with intravenous diltiazem: IV Diltiazem Study Group. Am J Cardiol 70:587–592
24. Glue P, Fang A, Gandelman K, Klee B (2006) Pharmacokinetics of an extended release formulation of alprazolam (Xanax XR) in healthy normal adolescent and adult volunteers. Am J Ther 13:418–422
25. American Society of Anesthesiologists. Basic standards for pre-anesthesia care. Chicago, IL: ASA; 2005. Available from: http://www.asahq.org/publicationsAndServices/standards [accessed 11/07/2009]
26. Hiew CY, Hart GK, Thompson KR, Hennessy OF (1995) Analgesia and sedation in interventional radiological procedures. Australas Radiol 39:128–134
27. Greenblatt DJ, Abernethy DR, Locniskar A et al (1984) Effect of age, gender, and obesity on midazolam kinetics. Anesthesiology 61:27–35