Safety of Transesophageal Echocardiography in Adults: Study in a Multidisciplinary Hospital

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Summary

Background: **TEE is a semi-invasive tool broadly used and its utilization associated to sedatives drugs might to affect the procedure safety.**

Objective: **to analyze aspects of TEE safety associated to the use of Midazolan (MZ) and Flumazenil (FL) and the influence of the clinical variables on the event rate.**

Method: **prospective study with 137 patients that underwent TEE with MZ associated to moderate sedation. We analyzed the following events: complications related with the topical anesthesia, with MZ use and with the procedure. Uni- and multivariate analyses were used to test the influence of the clinical variables: age, sex, stroke, myocardiopathy (MP), duration of the test, mitral regurgitation (MR) and the MZ dose.**

Results: **All patients (65±16 yrs; 58% males) finished the examination. The mean doses of MZ and FL were 4.3±1.9 mg and 0.28±0.2 mg, respectively. The duration of the examination and the mean ejection fraction (EF) were 16.4±6.1 minutes and 60±9%, respectively. Mild hypoxia (SO2<90%) was the most common event (11 patients); 3 patients (2%) presented transient hypoxia due to upper airway obstruction by probe introduction and 8 (5.8%) due to hypoxia caused by MZ use. Transient hypotension (SAP<90mmHg) occurred in 1 patient (0.7%). The multivariate analysis showed that severe MR, MP (EF<45%) and high doses of MZ (>5mg) were associated with events (p<0.001). The EF was 40%, in the group with MP and 44% in the group with severe MR and it can be a factor associated with clinical events in the last group.**

Conclusion: **TEE with sedation presents a low rate of events. There were no severe events and there was no need to interrupt the examinations. (Arq Bras Cardiol 2009; 93(5) : 443-447)**

Key Words: **Echocardiography, Transesophageal; Safety; Midazolam; Flumazenil.**

Introduction

In recent years, the transesophageal echocardiography (TEE) became a broadly used assessment tool in the investigation of cardiac and noncardiac diseases, being a complementary option to the transthoracic echocardiogram (TTE). The images of the heart through the esophageal technique have better definition and quality, allowing a detailed visualization of the heart structures, such as atrial appendices, valves and great vessels. Consequently, the TEE contributes with additional diagnostic information, when compared to the TTE[1-3]. However, the TEE is a semi-invasive examination, which requires sedation most of the times and can lead to complications related to the procedure itself or the use of sedation. Some studies have analyzed the risks of performing this procedure[4,5]. The objective of this study was to analyze the aspects of feasibility, safety and complication rates of TEE associated to the routine use of mild and moderate sedation.

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Methods

From October 2006 to July 2007 137 TEE were performed in our institution. All examinations were carried out at the Laboratory of Echocardiography, Emergency Room (ER) or Intensive Care Unit (ICU) of Hospital Israelita Albert Einstein (HIAE). A Phillips echocardiography equipment, model HDI 5000 with multiplane probe MPT 7-4 MHz and adequate software to perform the transesophageal echocardiography. Contraindications were relative: late esophageal surgery, previous high digestive bleeding, cervical column disease, dysphagia symptoms; and absolute: obstruction or critical stenosis of the esophagus, active high digestive bleeding, esophageal fistula, ulceration or perforation, esophageal diverticulum, esophageal tumor.

All patients had been fasting for 6 hours or more and had no complaints regarding deglutition of foods and no contraindications to the examination. The patients were maintained with a nasal oxygen catheter at 3 l/min and continuous pulse oximetry to monitor oxygen saturation.

After peripheral venous access had been attained, all patients received, before the examination started, progressive doses of Midazolan via I.V. route, until mild or moderate sedation was obtained, according to the line of procedure for anesthesia and sedation of Hospital Israelita Albert Einstein, classified in three levels, according to the following description:

ANSIOLYSIS (MILD SEDATION): it is the state of tranquility and serenity induced by drugs, during which the patient responds normally to verbal commands. Although the cognitive and coordination functions may be impaired, the cardiovascular and respiratory functions are preserved.

MODERATE SEDATION ("CONSCIOUS SEDATION"): it is a depression of consciousness induced by drugs, during which the patient awakes intentionally to a verbal command or slight tactile stimulus. No intervention is necessary to maintain the airway permeable and the spontaneous ventilation is adequate. The cardiovascular function is preserved.

DEEP SEDATION: it is a depression of consciousness induced by drugs, during which the patient does not awake easily; however, the patient responds to repeated painful stimuli. The capacity to maintain the spontaneous respiratory capacity can be impaired. The patient might require assistance to maintain airway permeability and/or respiratory support. The cardiovascular function is often preserved.

The local anesthesia of the oropharynx was carried out with 10% spray and 2% gel lidocaine. The heart rate (HR) and blood pressure (BP) were monitored with a Hewlett Packard automatic measurement equipment. The measurements were carried out in the brachial region every 5 minutes, from the beginning of sedation until the end of the examination. Cardiopulmonary resuscitation material with vasoactive drugs and orotracheal aspirator was available at the room throughout the examinations. Microbubble test (saline solution agitated in a syringe with 5 ml of 0.9% of saline solution + 1 ml of air, connected to a three-way cannula together with an empty syringe, with fast passage of solution from one syringe to another) was used to assess cardiac shunt. At the end of the procedure, the presence of bleeding, signs of local trauma, vital signs and complete recovery of the level of consciousness were verified. Flumazenil I.V. was used in some patients to revert sedation, according to the discretion of the examiner. All events and complications during the procedures and sedation were recorded in a spreadsheet, as well as the regular recording of BP and oxygen saturation. After the examination, all outpatients were discharged with a companion and advised about the late effects of the sedative and its restrictions.

The complications related to the examinations were characterized according to the following events:

1-complications with topical anesthesia: arrhythmia, laryngospasm, vocal cord paralysis;

2-complications with Midazolan: hypotension (systolic BP < 90 mmHg), paradoxical reaction, mild hypoxia (SO2=81-89%), severe hypoxia (SO2<80%), respiratory depression; 3-complications with flumazenil: hypertension or hypotension; 4-complications with the procedure, considering (4A)- minor complications: failure, intolerance, nausea, vomiting, bloody sputum, mild hypoxia, nonsustained ventricular arrhythmia, supraventricular arrhythmia; and (4B)- major complications: active bleeding, bronchospasm, esophageal lesion, heart failure, ventricular arrhythmia and others.

Therefore, some indices were defined for the complications related to the procedure and the medications. The complication index was defined by the equation: Number of complications/ Total number of TEE under sedation (NC/TNT).

All examinations were recorded in VHS tapes or DVD and the reports were typed and stored in a server database.

All patients received previous information about the examination and agreed with the terms of the Free and Informed Consent Form for the procedure and sedation, according to the Technical Norm, Resolution SS -169 de 19/06/1996.

Some clinical characteristics and procedure features were analyzed:

1- Age

2- Sex

3- Myocardiopathy (EF< 45%)

4- Presence of severe mitral regurgitation

5- Presence of previous stroke

6- Dose of Midazolan

7- Duration of the examination

Fisher's exact test (univariate analysis) and analysis of correspondence (multivariate analysis) were used to study the association between the variables of interest in the study[6].

Results

The examinations had the following indications: search for thrombi and emboligenic source (56%), assessment of heart valves and valvular prostheses (20%), suspected endocarditis (14%), assessment of aortic pathologies (4%), evaluation of intracardiac masses (1.5%) and others (3.5%).

Midazolan was used in all patients, whereas flumazenil was prescribed to 85 patients (62%), according to the discretion of the examiner. It was not necessary to use flumazenil for the urgent reversion of sedation in any of the patients in this series. The mean doses of Midazolan and Flumazenil were 4.29±1.87 mg and 0.28±0.24 mg, respectively; mean age was 65.04±15.94 years and 58% of the patients were males; the mean duration of the examination was 16.42±6.18 minutes; EF was 60%±9; the mean EF in the group with myocardiopathy was 40%±4 and the mean EF in the group with severe mitral regurgitation was 44%±5.

According to the classification used, we obtained the following results:

Complications with the procedure: minor events occurred in three cases and were caused by mild and transient hypoxia, due to the transient obstruction of the upper airway by the base of the tongue or mechanical obstruction by the space occupied by the probe during its introduction. It was not necessary to interrupt the examination, administer flumazenil to reverse sedation or use ventilatory support.

They represented approximately 2% of the cases. According to the American Heart Association (AHA), the expected rate of events is approximately 3.3%[7]. Major events (severe ones)

were not observed in this series. According to the American Heart Association (AHA), the acceptable rate is around 0.5%[7]. Complications due to the use of Midazolan occurred in 9 cases, with 8 due to mild hypoxia (5.8%), i.e., levels of oxygen saturation between 81 and 90%. All cases of mild hypoxia related to the use of Midazolan quickly responded to the increase in oxygen supply and neither the test interruption nor the sedation reversal with flumazenil was necessary. Arterial hypotension (SAP=80-89 mmHg) occurred in 1 case (0.7% of the cases); it was transitory and the sedation withdrawal and reversal with flumazenil was not necessary. No respiratory failure, paradoxical reaction or intolerance to Midazolan was reported. These events corresponded to 6.5% of the cases, with the acceptable rate in the literature being a maximum of 10%[8]. No complications were observed with the use of topical anesthetic or flumazenil.

No significant difference was observed between the doses of Midazolan in the groups with and without severe MR (5.08±2.30 x 6.75±2.06, p=0.15) (Table 2), and in the groups with and without myocardiopathy (5.08±2.25 x 5.73±2.94, p=0.37) (Table 3). However, a significant difference was observed regarding Midazolan doses in the group of patients older than 65 years, when compared to those younger than 65 (4.2±1.8 mg x 6.2±2.3 mg, p<0.01).

The results presented in Table 1 and Chart 1 allows us to affirm that there is an association between the rate of complications and the following variables: Midazolan dose, severe MR and ejection fraction. No association was observed between events and the following clinical variables: age, sex, previous stroke, test duration > 10 minutes.

Table 1 - Descriptive levels of the association study between each variable of interest and the occurrence of complications during the procedure.

Variable	Descriptive level
Age	0.203
Stroke	0.737
Midazolan dose	0.004
Test duration	0.128
Sex	0.535
Severe MR	0.001
Ejection fraction	0.001

MR -mitral regurgitation

Table 2 - Descriptive measurements of the Midazolam dose in the groups with and without severe MR (p=0.15).

Severe MR	Mean dose	SD
No	5.08 mg	2.30
Yes	6.75 mg	2.06

MR -mitral regurgitation

Table 3 - Descriptive measurements of the Midazolam dose in the groups with and without myocardiopathy (p=0.37).

EF<45	Mean dose	SD
No	5.08 mg	2.25
Yes	5.73 mg	2.94

EF - ejection fraction

Discussion

The complications related to the TEE might be due to the passage and handling of the esophageal probe during the procedure and the use of sedatives and other medications. In this study, the rate of complications related to TEE was low, lower than the one observed in the literature[7,8]. Complications such as bleeding, respiratory failure, heart failure, arrhythmia or death were not observed. In a study about the safety of TEE in approximately 10,000 patients, the authors reported pulmonary and heart complications, as well as bleeding in 0.18% to 0.5% of the cases and death in 0.098% of the cases, similar to the rates observed in series with more than 200,000 patients submitted to gastroduodenoscopy procedures. It is worth mentioning that, in this study[5], the majority of the patients was awake and did not receive sedation and therefore, did not meet the criteria of moderate sedation used and aforementioned in our study.

The failure during the insertion of the esophageal probe was not observed in the 137 procedures and seems to be related to factors such as the patient's cooperation, degree of sedation and the operator's experience. There are reports in the literature of failure rates being related to the number of procedures performed, i.e., centers that performed fewer than 200 examinations/year have failure rates of 3.9±3.2%, when compared to centers that perform more than 200 examinations/year (1.4±0.9%, p<0.05)[5]. However, in this study, as the examinations were performed by experienced physicians supported by an efficient nursing team and a careful use of sedation, no failures were observed.

Another aspect is related to the possibility of thermal lesions and mucosal lacerations due to the extended use of the esophageal probe, such as during cardiac surgeries. The literature has reported the presence of thermal lesions and bleeding in anticoagulated patients, and more rarely, mucosal damage in patients with Mallory-Weiss esophagitis[9-11]. The curling of the probe during handling is an unusual situation and can cause difficulty at the removal. In these circumstances, the probe must be introduced until the stomach, where the curling can be undone. Compression of adjacent structures has been reported in procedures carried out in children, such airway obstruction[12]. None of the conditions described above was observed in our study.

Other complications, also related to the procedure, include the supra-ventricular and ventricular arrhythmias, which are most of the time, self-limited[13]. These arrhythmias are many times caused by the handling of the esophageal

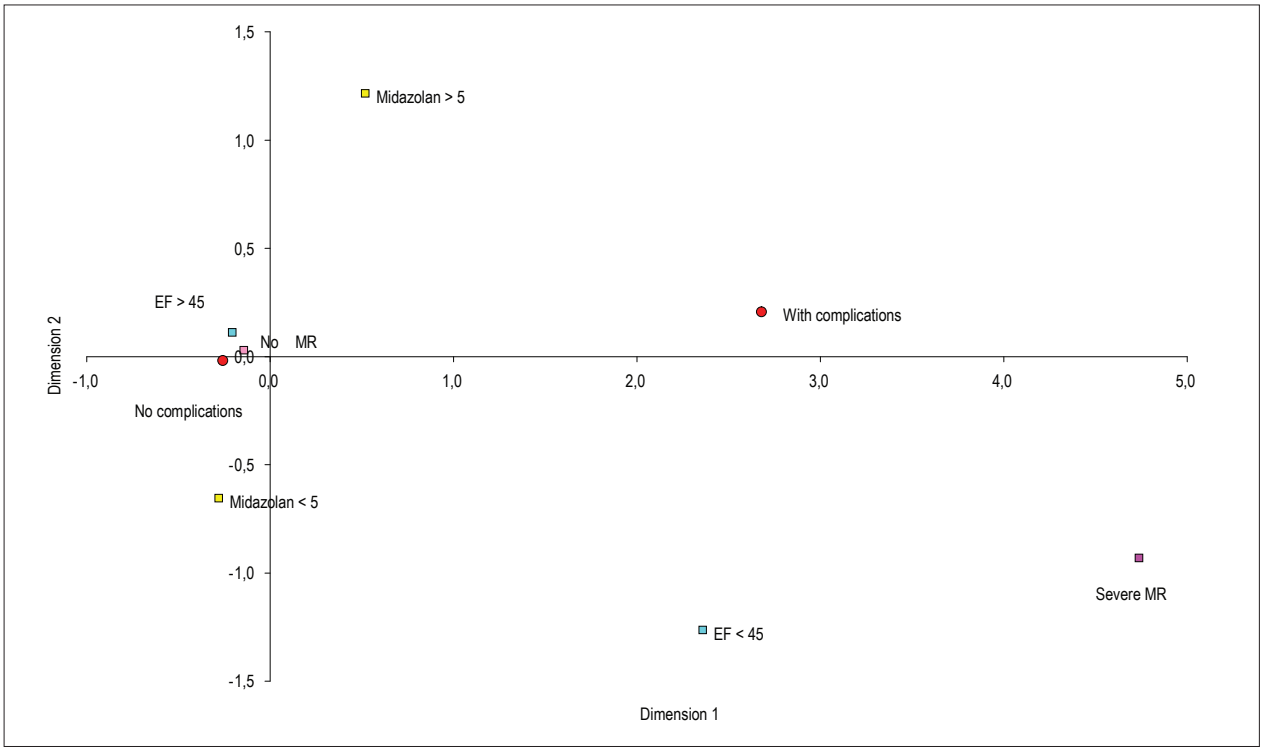

Chart 1 - Correspondence analysis chart. Multivariate analysis showing the occurrence of complications and the variables: ejection fraction (EF), severe MR and Midazolan dose > 5 mg.

probe during the procedure, mainly in patients without sedation or under superficial sedation, and anti- arrhythmic agents are rarely used. The bradyarrhythmias are also rare and are related to the vagal effect during the procedure. They are usually self-limited and it is rarely necessary to use atropine. There are reports in the literature of death due to ventricular arrhythmia in a patient submitted to TEE. The autopsy revealed an infiltrate of lymphocytes in the myocardium, suggesting active myocarditis[14]. Pulmonary complications such as bronchospasm and laryngospasm are mentioned in the literature. They occur in approximately 0.2% of the procedures and are probably caused by the probe handling or medication. Hypoxia usually occurs caused by two situations: 1 – hypoxia related to the procedure (high airway obstruction by the base of the tongue or mechanical obstruction by the space occupied by the probe) and 2 – hypoxia caused the sedative[15]. Contrarily to the hypoxia related to the procedure, which usually occurs at the beginning of the procedure, soon after the passage of the esophageal probe, the hypoxia related to the use of sedation occurs during the examination, some minutes after the passage of the probe, and is related to secondary hypoventilation to the sedative effect, as Midazolan has a 3-minute start action and a 5-minute maximum effect, after which its effect declines gradually in up to 30-40 minutes.

It is at the peak moment of the pharmacological action that we can verify the presence of hypoxia due to hypoventilation. In our study, the analysis of the events occurred in a small percentage of patients and it was not necessary to interrupt any of the examinations; these data are in agreement with those in the literature[13]. Heart failure rarely occurs in patients with advanced myocardiopathy submitted to TEE and it is due to the withdrawal of medication, the endogenous stimulation of catecholamines and the use of sedation, which can contribute to the worsening of the ventricular contractile function.

Severe bleedings are also rare and the risk is higher in patients with esophageal disease (diverticulum, tumors and stenosis). In an european multicenter study, a death caused by acute bleeding was reported in a patient with esophageal neoplasia. During the passage of the probe, there was laceration of the tumor with important hematemesis[5]. Another example of severe bleeding after TEE was reported in a patient that received thrombolytic agents for the treatment of thrombosis of a mechanical mitral prosthesis. This patient presented hemothorax due to an esophageal hematoma that ruptured into the thorax[5].

Some variables such as the use of Midazolan > 5 mg, myocardiopathy and severe MR were associated with a significantly higher number of complications during the procedure, at the uni- and multivariate analysis. Midazolan is a benzodiazepine agent with liver metabolism and practically renal excretion. The half-life is around 1-4 hours and it is increased in both kidney, heart and liver failure, as well as in obese and elderly patients. Hemodynamic and respiratory events, among others, are known to occur with the use of Midazolan.

More common in children and in patients with hemodynamic instability, hypotension and respiratory depression frequently occur when associated with narcotics.

The recommended Midazolan dose is 0.5-2 mg I.V. in 2 minutes; the effects must be assessed every 2-3 minutes and the total recommended dose is usually 2.5-5 mg. The association of other central nervous system depressors, elderly patients and those with kidney, heart or liver failure must be monitored and lower doses are indicated. The effects on the cardiovascular system are usually caused by a decrease in the peripheral vascular resistance, myocardial depression and decreased cardiac output[8].

The severe MR promotes a volumetric overload to the left chambers and, consequently, an increase in the left ventricular diastolic-end pressure, which can lead to pulmonary congestion.

The mean EF in the group with myocardiopathy was 40%±4 and 44%±5 in the group with severe MR. Therefore, we observed that the group with severe MR also presented a reduced mean EF (44%±5) and this can be an associated factor in the occurrence of events. However, no significant difference was observed between the doses of Midazolan in the group with and without severe MR (5.08±2.30 mg x 6.75±2.06 mg, p=0.15) (Table 2) and in the group with and without myocardiopathy (5.08±2.25 mg x 5.73±2.94 mg, p=0.37) (Table 3).

Conclusion

The present study demonstrates that when the TEE is performed by experienced professionals, even in patients under sedation, it is associated with a low risk of events. No major events were reported and there was no need to interrupt the procedures due to minor events, guaranteeing the safety of the procedure.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

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