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Cardiorespiratory complications of digestive endoscopy not related to sedation

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ABSTRACT
Although digestive endoscopy is considered to be a safe procedure, both the growing complexity of the techniques and the underlying diseases of patients increase the risk of adverse events during the procedure. Cardiorespiratory events are the most frequent complications, and can occur in patients with or without sedation, although they appear more often when the patient is sedated. The body’s physiological response to stress is what causes these adverse events, which are generally mild and transient, although they can be serious. They are more frequent in patients with cardiopulmonary diseases, which logically increase risk. The autonomic nervous system, through its sympathetic and parasympathetic branches, is primarily responsible for these alterations. Patients with asthma or chronic obstructive pulmonary disease have a higher risk of hypoxemia, bronchospasm, and arrhythmia during the endoscopic procedure. Patients with arrhythmia and ischemic heart disease have a higher risk of myocardial ischemia and heart rhythm disturbances. The risk of adverse events during the procedure can be reduced by reviewing the patient’s
medical history along with a basic clinical examination before endoscopy. A brief interrogation about symptom control can also help the safety of endoscopy.

**Keywords:** Digestive endoscopy. Endoscopy complications.

**INTRODUCTION**

Digestive endoscopy (DE) currently plays a fundamental role in the diagnosis and treatment of multiple diseases of the digestive tract, and is considered as a very safe procedure (1,2). However, increased complexity, both in terms of techniques and patients themselves (elderly, pluripathological, receiving anticoagulant and/or antiplatelet therapy), carries a greater risk of suffering adverse events during the procedure.

Most of the publications that analyze the complications of DE focus on those related to sedation and the technique itself, especially in terms of therapeutic procedures (perforation, hemorrhage, etc.), while those evaluating the cardiorespiratory complications (CRC) of DE *per se* are less common, older, and less known but no less important for the endoscopist. The objective of this review is to give the endoscopist an overview of the main CRC of DE, which may lead to gaining a better understanding of their pathophysiology and risk factors, in order to establish measures to prevent them.

Various studies have evaluated the risk of CRC during DE, establishing a frequency between 0.017 % and 0.54 % (2-5). More recently, Sharma et al. estimated a frequency of CRC close to 1 %, with this group representing more than half of the adverse events recorded during a DE procedure, in addition to being the primary cause of procedure-related mortality (6). These discrepancies between the results of different studies (due to their design, definition of CRC, population studied, and sedation status) make it difficult to assess the real incidence of these adverse events (7).

The pathophysiological changes most frequently recorded during DE are those that occur in blood oxygen saturation levels, blood pressure, or heart rate, which in most cases are mild and transient but may become fatal (6-10) (Table 1). These changes may appear in healthy subjects, triggered by the body’s physiological response to the stress
caused by the endoscopic (invasive) procedure, or else occur in patients with morbidities that play a role as risk factors (8,9,11-13). In addition, there are risk factors inherent to the procedure itself, such as duration or the use of endoscopes with larger diameters (9,10). Table 2 summarizes the main risk factors for the occurrence of CRC during DE.

In a retrospective study that analyzed events that required cardiopulmonary resuscitation (CPR) maneuvers in the endoscopy units of several South Korean hospitals, it was observed that most events occurred during the endoscopic procedure, particularly during the exploration of the upper digestive tract. In addition, these events were generally due to an exacerbation of an underlying disease, with respiratory failure being the main trigger of CPR (14). The authors estimated an incidence rate of 15 cases per 100,000 endoscopies for events that required CPR, with a mortality rate of 6 per 100,000 cases for these events (14).

PATHOPHYSIOLOGICAL CHANGES DURING DIGESTIVE ENDOSCOPY

Hypoxemia is one of the main adverse events that may occur during DE, mainly during upper GI endoscopy (EGD), and is aggravated by endoscopes with a larger diameter, the existence of underlying cardiopulmonary diseases, as well as the use of sedative medication (9,11-13,15). It is thought that the passage of the endoscope produces a partial obstruction of the airway, which leads to desaturation and hypoxemia, even in subjects without other risk factors (9,16). In addition to those previously mentioned, Alcain et al. identified as predictive factors for hypoxemia during DE a baseline saturation of less than 95%, repeated esophageal intubation attempts, emergency procedures, and an American Society of Anesthesiology (ASA) classification greater than or equal to three (17).

The autonomic nervous system (sympathetic and parasympathetic) plays a fundamental role in the body’s response to endoscopic procedures. The stimulation of receptors at the level of the oropharynx and hollow viscera, in the case of DE, mainly by mechanical stimuli, triggers different physiological responses (18,19). Best known is the vasovagal response, which through the parasympathetic nervous system (PSNS) causes bradycardia and hypotension in response to the mechanical stimulus produced
by the passage of the endoscope through the oropharynx or the hollow abdominal viscera distended with air insufflation (8,18,19). On the other hand, the stress to which the organism is subjected during the procedure, or the anxiety that endoscopy generates in the patient, triggers an activation of the sympathetic nervous system (SNS), in charge of preparing the organism for a stress situation, causing tachycardia, hypertension, and sweating (11,18,19). The pain that sometimes appears during the procedure usually causes a sympathetic response, although it can also produce a parasympathetic response through the vasovagal reflex (10,19).

The changes in heart rhythm that occur during DE are considered to be a consequence of the autonomic nervous response and hypoxemia caused by the passage of the endoscope through the oropharynx (9,11,20). The alteration of the sympathetic-vagal tone favors the appearance of arrhythmias, and hypoxemia induces cardiac ischemia, which in turn favors the appearance of electrical changes (13,21,22). However, some studies have shown that there is no significant correlation between hypoxemia and the development of electrocardiographic abnormalities, concluding that their appearance is due to increased cardiac workload (11,12). These studies coincide in identifying patients with underlying heart or respiratory diseases as a population at risk for the development of arrhythmias during the procedure (9,11,12).

RECOMMENDATIONS FOR ENDOSCOPIC PROCEDURES IN HIGH-RISK PATIENTS

Before performing any endoscopic procedure, it is necessary to categorize the patient according to the risk of developing a cardiorespiratory event during DE. This requires a review of their medical history and a basic clinical examination. In addition to this, for those that are considered to be high-risk patients (cardiac, bronchial conditions), it is advisable to conduct a brief interview focusing on the presence of symptoms in the hours before the procedure, current medical treatment, and even the date of the last follow-up visit with the specialist.

The physical status classification system of the ASA is widely used to assess the status of a patient’s health in order to estimate their surgical risk (23) (Table 3). The STOP-BANG questionnaire also helps to easily and quickly identify patients with obstructive sleep apnea syndrome (OSAS) (24) (Table 4). These two tools help alert the
endoscopist at the endoscopy room about those patients who have a higher risk of developing adverse events during the endoscopic procedure.

Although there is no general consensus as to its indication (7), pulse oximetry monitoring is recommended for all high-risk patients who are going to undergo an endoscopic procedure, regardless of whether they will receive sedation or not (17,25). In patients with known heart disease electrocardiographic monitoring is also recommended (11,26).

There are discordant results regarding the benefit of administering supplemental oxygen to reduce the risk of CRC in sedated patients undergoing endoscopic procedures (6), results that could be extrapolated to non-sedated patients.

**Asthma**

Patients with bronchial asthma have a number of structural changes derived from chronic inflammation of the airway, which causes greater resistance to air flow, along with greater sensitivity and bronchial reactivity to external stimuli (27). Certain chemical and mechanical stimuli, such as the passage of the endoscope through the oropharynx or the passage of secretions into the airway, activate the nerve receptors distributed throughout the airway, triggering an exacerbated bronchoconstriction reflex response in these patients, which is mediated by the PSNS (28). It is estimated that the risk of bronchospasm in the perioperative period of asthmatic patients ranges from 0.17 % to 4.2 %, the main risk factors being the proximity of an asthma crisis to the time of procedure, poor clinical control of the disease, and use of sedative drugs (29-31).

Optimal disease control is necessary to reduce the risk of bronchospasm during EGD. It has been observed that the use of β₂-agonists before the procedure can decrease the bronchoconstriction reflex with oropharyngeal manipulation (32), and thus treatment with β₂-agonists and corticosteroids in high-risk patients is recommended (29,32). In these patients, it is necessary to question them about recent respiratory infections, triggers, and degree of clinical-functional control of the disease due to their implications for the occurrence of complications during the procedure (29).
Chronic obstructive pulmonary disease (COPD)
Several studies have shown that patients with COPD experience episodes of desaturation and arrhythmia more frequently during EGD without sedation than patients without a history of respiratory disease (9,12,13,17). In addition to the partial obstruction of the airway during EGD, and the passage of secretions, it is thought that an alteration in the ventilation/perfusion relationship may contribute to this condition (17).
Patients with respiratory conditions and baseline saturation below 95 % at the time of EGD have a higher risk of CRC during the procedure (17), so it may be prudent to defer the exploration in these cases.
Similar to asthmatic patients, recent infectious exacerbations, as well as the degree of clinical-functional control of the disease, are worth noting, and it is thus recommended that the treatment of the underlying disease be optimized before performing the procedure to reduce the risk of adverse events during DE.

Arrhythmias
Heart rhythm disturbances during DE are more frequent in patients with ischemic heart disease or valvular heart disease as compared to non-cardiac subjects (9,22,33,34), and as previously mentioned, in those with COPD. Sinus tachycardia and ventricular extrasystoles are the main arrhythmias detected, usually without clinical significance when they are self-limited and have no hemodynamic repercussion (6,9,10).

Ischemic cardiomyopathy
In patients with ischemic cardiomyopathy (IC), changes in the ST segment that may be present in patients with IC during ED are especially relevant, since they are considered as clinically significant for myocardial ischemia. Classically, it was thought that this ischemia was secondary to hypoxemia, when the development of electrocardiographic abnormalities coincided with desaturation episodes (22,33). However, some studies have questioned the existence of a significant correlation between ischemia and hypoxemia, suggesting that ischemia is secondary to an increase in myocardial oxygen
demand as a result of increased cardiac workload during DE, similar to what happens during a stress test (11,12,33,35). In most cases these electrical changes do not have any clinical correlates (34,35).

There is currently no consensus as to the optimal waiting time required to safely perform an endoscopic procedure in patients with recent acute coronary syndrome (ACS). In scheduled endoscopic examinations it may be prudent to defer the procedure a few months after the ischemic event, a strategy that is not feasible in urgent cases.

Tseng et al. observed that patients with stable IC who had an urgent EGD procedure for upper gastrointestinal bleeding (UGIB) at least 60 days after an ischemic event had a higher incidence and frequency of ventricular arrhythmias than the healthy control group, also observing that in these patients more frequent electrical changes may be seen in the electrocardiogram (ST depression) without development of angina or infarction during or after the procedure (34). Spier et al. reported an inversely proportional relationship between DE complications and proximity to an ischemic event: among 135 patients, the only ones who developed complications were those in whom the EGD had been performed on the same day as the ACS, and no complications were recorded in those who had an EGD at least 24 hours after an ACS (36). A recent systematic review by Canadian authors established the use of sedative drugs during the endoscopic procedure, in addition to the temporal relationship between the ischemic event and DE, as a risk factor for the development of cardiorespiratory complications in these patients (26). In this review, the risk of cardiovascular complications related to DE is estimated at 9.1 % after an ACS, with the risk of death attributed to DE being 3.7 % of total complications (26).

In patients with a recent ACS, an optimal anticoagulant and antiplatelet therapy is recommended, together with the use of proton pump inhibitors (PPIs), to attempt to reduce the risk of bleeding and thus reduce the chances of an emergency EGD procedure, which in turn might trigger other complications (26). In cases where EGD is unavoidable, it may be useful to use agents such as hemostatic powders (Hemospray®), which allow rapid hemostasis, to reduce endoscopic time and thus decrease the likelihood of CRC (26).
CONCLUSIONS

DE is considered to be a safe procedure with few contraindications. However, even in the absence of comorbidities or external factors such as the use of sedatives, the body’s own physiological response to the different stimuli derived from the procedure can trigger cardiorespiratory adverse events. These are generally mild and self-limited; however, sometimes they may have serious consequences, especially in risk groups. The autonomic nervous system is the main system involved in said response. Patients with asthma and/or COPD have a higher risk of hypoxemia and bronchospasm during the endoscopic procedure when compared to the general population. Likewise, patients with a history of cardiac arrhythmias or ischemic heart disease have an increased risk of arrhythmia and myocardial ischemia during DE. In these patients it is essential to take precautions before, during, and after the procedure in order to reduce adverse events and to allow taking quick, effective action should these develop.

REFERENCES


Table 1. Principal cardiorespiratory complications of digestive endoscopy

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Hypoxemia</th>
</tr>
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<tbody>
<tr>
<td>Hypotension</td>
<td>Hypercapnia</td>
</tr>
<tr>
<td>Sinus tachycardia</td>
<td>Aspiration pneumonia</td>
</tr>
<tr>
<td>Sinus bradycardia</td>
<td></td>
</tr>
<tr>
<td>Extrasystoles</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
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<tr>
<td>Supraventricular tachycardia</td>
<td></td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td></td>
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<tr>
<td>Myocardial infarction</td>
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</tbody>
</table>
Table 2. Principal risk factors for the appearance of cardiorespiratory complications during digestive endoscopy procedures

<table>
<thead>
<tr>
<th>Risk factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 65 years</td>
<td>Prolonged procedure time</td>
</tr>
<tr>
<td>ASA ≥ 3</td>
<td>Supine position</td>
</tr>
<tr>
<td>Oxygen saturation &lt; 95 %</td>
<td>Difficult esophageal intubation</td>
</tr>
<tr>
<td>Pre-existing cardiopulmonary disease</td>
<td>Emergency procedure</td>
</tr>
<tr>
<td></td>
<td>Use of sedative medication</td>
</tr>
</tbody>
</table>
### Table 3. American Society of Anesthesiology (ASA) Classification System

<table>
<thead>
<tr>
<th>ASA Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Healthy patient not undergoing elective surgery</td>
</tr>
<tr>
<td>II</td>
<td>Patient with mild, controlled, and non-disabling systemic disease</td>
</tr>
<tr>
<td>III</td>
<td>Patient with severe but not disabling, systemic disease</td>
</tr>
<tr>
<td>IV</td>
<td>Patient with severe and disabling systemic disease, which also constitutes a constant threat to life and cannot always be corrected through surgery</td>
</tr>
<tr>
<td>V</td>
<td>Terminal or dying patient, whose life expectancy is not expected to exceed 24 hours with or without surgical treatment</td>
</tr>
<tr>
<td>VI</td>
<td>Patient declared brain-dead, treated with support measures to remove organs for transplantation</td>
</tr>
</tbody>
</table>
### Table 4. STOP-BANG Questionnaire

<table>
<thead>
<tr>
<th><strong>Snoring</strong></th>
<th>Do you snore loudly?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tiredness</strong></td>
<td>Do you often feel tired, fatigued, or sleepy during daytime?</td>
</tr>
<tr>
<td><strong>Observed</strong></td>
<td>Has anyone observed you stop breathing during your sleep?</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td>Do you have or are being treated for high blood pressure?</td>
</tr>
<tr>
<td><strong>Body mass index (BMI)</strong></td>
<td>Body mass index over 35 kg/m²?</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Age over 50 years old?</td>
</tr>
<tr>
<td><strong>Neck</strong></td>
<td>Neck circumference &gt; 40 cm?</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male?</td>
</tr>
</tbody>
</table>

Risk of obstructive sleep apnea syndrome: low (answered yes in 0-2 questions), intermediate (answered yes in 3-4 questions), high (answered yes in 5-8 questions).